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THE
ELECTRONIC THEORY
OF
ORGANIC CHEMISTRY

BY

M. J. S. DEWAR

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FOREWORD

During the last twenty-five years the writer has had constantly in mind the desirability of a fuller exposition of what may be termed the Lapworth–Robinson system of organic chemical theory; for one reason or another the project was never brought to fruition.

At last an opportunity seemed to present itself in a joint work with Dr. M. J. S. Dewar which was actually commenced in 1946.

But this collaboration broke down for several good reasons. Thus Dewar was so active that it was not possible to keep pace with him; he proved not only well versed in modern wave mechanics of the atom but also capable of making new uses of these powerful methods; he developed novel points of view over the whole range of topics treated. In fact it was clearly Dewar's work.

The outcome is a connected series of original essays, and I commend it to students as the best available account of modern theories of the mechanism of the reactions of carbon compounds. Certain suggestions that are included can be criticized, but that is inevitable, and this stimulating book unquestionably represents a further step forward in our grasp of the complex problems of the relation of structure to reactivity.

Because of the early history of the work it became an account of the present position as the author sees it; there is no doubt that I was expected to contribute explanations of the experiments and theories of 1920–30, of which later developments have occurred in so many directions. In the chapters that follow, a knowledge of the early work is often assumed or is taken to be part of a generally accepted system and specific references are sometimes omitted. As a grossly exaggerated parallel, the atomic theory is now used without a reference to Mr. Dalton or any of the Greek philosophers. Nevertheless we are not so far away from the origins in the present case and I regret that owing to my backsliding a fuller treatment of those aspects was not possible.

No attempt can be made to repair the damage in a foreword, but it is a privilege to be allowed to indicate some of the broad ideas introduced in the decade 1920–30.

Even after the main lines of the constitution of the atom became clear, the vague notion of 'chemical affinity' survived and was contrasted, or combined, with effects supposed to be electrical in origin.

Chemists were loth to relinquish the conception of some special chemical force, which seemed to be demanded by the perplexing caprices encountered in practice, and by the incalculable varieties of qualities of elements and their compounds. It was as necessary to abandon this hypothesis, and to seek physical interpretations based on atomic electrical theory, as it was to leave behind the view that syntheses in living organisms involve the operation of a 'vital force'.

The earlier exponents of the electronic theory of valency undoubtedly gave a longer lease of life to 'chemical affinity' because of the rigidity and too great precision of their views. There was clearly some inadequacy, some failure of scope and adaptability, and the cause of this was only gradually revealed with the advance of our knowledge of the atom and of the electron. There is, of course, still very much to be done in resolving apparent anomalies in connexion with comparative reactivity, but no one now doubts the possibility of such explanation.

The writer's Faraday Lecture of 1947 was designed to show how an electrochemical theory of reactivity was extended from such an obvious case as the correlation of the strengths of acids and bases to the interpretation of the data relating to the orientation and behaviour of substituents in the aromatic nucleus. Stress was laid on the experimental foundations of these theories, such as the *m*-nitration of benzyltrimethylammonium nitrate, the C-alkylation of substituted β-aminocrotonic esters, the additive reactions of αβ-unsaturated ketones, and similar observations.

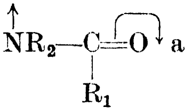
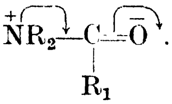
Put very briefly in the form of propositions the qualitative theory included the following, which, however, does not constitute anything like a complete statement.

1. Anions, cations, and radicals are taken as the guides to types of reactivity.

2. Anionoid and cationoid reagents are such as exhibit reactivity of anionic and cationic type respectively. This is recognized as electron donor (anionoid, nucleophilic) and electron acceptor (cationoid, electrophilic) in character and implies reactivity due to unshared electrons on the one hand, and incomplete outer-electron configurations of the atoms on the other.

3. Reaction cannot occur unless the freeness and incompleteness of (2) exists, and activation often brings about such a prerequisite polarization. Thus the carbonyl group is, or becomes, $\rangle\mathrm{C}\overset{\curvearrowright}{=}\mathrm{O}$, in which the arrow symbolizes a break away of electronic atmosphere (to an unknown extent) from carbon, which thus acquires cationoid character.

4. The general electric effect (Lewis) is a displacement which may have a great influence in modifying reactivity but does not itself produce unshared electrons or incomplete configurations, and hence does not provide the conditions necessary for reactivity. This statement requires a longer discussion and much amplification. In some extreme cases (such as CI_4) the general effect seems to be accompanied by changes in co-valency, that is, in electron-sharing relations. On the whole it is salutary to maintain the distinction between the general electrical effect and those processes which involve changes in electron-sharing.

5. Conjugative polarization occurs when a cationoid centre is contiguous in a molecule to an anionoid centre and internal satisfaction of the two types of reactivity occurs. This results in a *neutralization* or *relay* of reactivity. Thus in $>C\overset{\curvearrowright}{=}O$, the carbon is cationoid and the oxygen is anionoid. But carbon is intensely reactive when its electronic configuration is depleted; whereas oxygen can bear a negative charge, which merely increases its basicity. Therefore the CO complex is characteristically cationoid. $R_3N\rightarrow$ (where $\rightarrow$ represents active, spearhead, unshared electrons) is strongly anionoid. If then one of the R groups is $CO\cdot R_1$, we have  $\overset{\uparrow}{N}R_2—C(R_1)\overset{\curvearrowright}{=}O$ and internal neutralization occurs as in  $\overset{+}{N}R_2\overset{\curvearrowright}{—}C(R_1)\overset{\curvearrowright}{=}\overset{-}{O}$. This is a dipole, a kind of betaine, in which the characteristic anionoid reactivity of $NR_3\rightarrow$ and the cationoid reactivity of $>C\overset{\curvearrowright}{=}O$ have been mutually satisfied.

Now the ethenoid group $C\overset{\curvearrowright}{=}C$ is recognized as *anionoid* under ordinary circumstances, for it seems that carbon can bear a depleted electron configuration better than unshared electrons; the latter are far more prone to exhibit reactivity. In the combination $C\overset{\curvearrowright}{=}C—C\overset{\curvearrowright}{=}O$ we can get internal neutralization $^{\gamma}C\overset{\curvearrowright}{=}C\overset{\curvearrowright}{—}{}^{\alpha}C\overset{\curvearrowright}{=}O$ as indicated by the new position of the larger arrow. This does not fully neutralize the carbonyl reactivity but relays the quality of the α-carbon atom to that in the γ-position.

Conjugative polarization covers a large field of organic chemistry, even if we consider only the possible combinations of the simpler anionoid and cationoid complexes.

6. In considering special problems it is usually preferred to analyse first the types of conjugative polarizations that are possible and probable. Afterwards the effect of general electrical displacements on these conjugated systems can be studied.

It was by following this method that the complex data of benzene substitutions could be collated. The whole theory had the great advantage that a clear division of the subject was possible according to the character of the reagent as anionoid or cationoid.

7. Polarization of unsaturated groups (in the sense of co-valency changes) and of conjugated systems was assumed to occur to some extent in normal molecules, a phenomenon later termed *mesomerism* and illustrated experimentally by researc[illegible] as that of Sutton on the comparison of the dipole moments of aromatic and related aliphatic or alicyclic compounds. To give only one illustration, the physical properties of amides show clearly their dipolar nature. In the course of reactions the

mesomeric process is assumed to go much farther and in fact usually becomes a completed transfer of electrons.

8. Application of the principles of anionoid and cationoid processes to the illustration of particular reactions becomes a very simple matter, often no more than a mere translation of an older theory. The positive and negative surroundings usually form part of a circuit through which a small current passes as the reaction is completed. The direction of this current is clear from the circumstances, including the character of any catalyst which is required, and interesting consequences ensue, for example, in regard to the polarity of migrating groups in molecular rearrangements.

9. In the elaboration of all electronic mechanisms the fundamental tenet of the older qualitative theory was that the electronic configurations of the atoms must be maintained with the original number of quantized electrons. In other words, the rare-gas electron atmosphere must be kept inviolate if possible; it occasionally had to be depleted but could never be augmented. It must be remembered that we are dealing chiefly with carbon, oxygen, nitrogen, and hydrogen.

This led automatically to the correct orientation of electron excess and defect in conjugated systems. The importance of this fundamental point is hard to overstress because many of the difficulties felt in the applications of the theory spring from a lack of appreciation of its significance.

10. The theory did not embrace any estimate of the extent of polarizations, simple or conjugated. It was, however, assumed that a small fraction of an electron could be operative in the *initiation* of a process and the idea of full ionization of carbon compounds, so prevalent to-day, was deprecated. Naturally there is no real objection to this as a limiting case, but the writer considers the present tendency to be retrograde, in that ionization, often a lazy way out of a more detailed study, is frequently assumed without proof and under circumstances in which the full process is highly improbable.

11. In some systems a vibration like that of a spring is postulated in order to make the assumption of large electronic displacements unnecessary. For example, in aromatic substitution, the type is maintained, and no great departure from it at any stage is required, provided we envisage an oscillation of electrons in the nucleus. Each swing in one direction enables the substituent to tighten its hold on the nuclear carbon; each swing in the other direction, relieving strain, allows the substituted proton to be released from the molecule.

It must be clear that many further special hypotheses emerged, but only one such will be mentioned here.

In an early paper Kermack and the writer suggested a principle of alternation of octet stability in a chain of atoms. The central idea was that shared electrons are unlikely to take part to an equal extent in the stability factors associated with the configuration of the two atoms concerned. This hypothesis was almost wilfully misunderstood as meaning electrostatic appropriation of the electrons by the stronger party and it was certainly misapplied by its authors. Nevertheless there seems some justification for it to be discerned in wave-mechanical theory, and an interesting development of the future may be to put the idea in its proper place in relation to alternative explanations of particular phenomena.

The writer has not attempted to do this because the distinct theory of conjugative polarization seemed to cover the same ground. It is hard to devise a crucial test.

In conclusion I wish all success to this latest effort to generalize our science in one of its most fascinating aspects. Gone are the days when organic chemistry could be stigmatized as 'memory' work and students who will allow Dewar to lead them through the newly won territory will soon see why that is true.

R. ROBINSON

PREFACE

THE electronic theory of organic chemistry was developed more than twenty years ago, the culmination of theoretical investigations by generations of organic chemists. It was essentially empirical in nature, being based on an intuitive picture of the atom which to-day seems crude and incomplete, and for this reason many chemists now tend to regard it with suspicion. Yet in practice the theory proved remarkably successful in unifying organic chemistry, and physical measurements have established the reality of the electronic processes which it had postulated.

The electronic theory was developed at a time when ideas about atomic structure were in a very primitive state. The Bohr theory, though superficially attractive, could give no valid account of the existence of molecules, much less of the details of their structure which were the main concern of the electronic theory. These shortcomings have been met in the new quantum mechanics of Heisenberg and Schrödinger, and it has now become abundantly clear that the earlier electronic theory was essentially correct in all its conclusions and that its theoretical foundation, borrowed from the Bohr theory, proved only a handicap.

This foundation now requires modification. The new quantum mechanics has proved so outstandingly successful in every case where its predictions can be adequately tested that it must be accepted as a basis for any theory connected with atomic or molecular structure. This task is less simple than it might appear. For although all chemical problems could in principle be solved by *a priori* quantum-mechanical calculation, in practice the mathematical difficulties are insuperable at present and exact solutions have been obtained only in a few especially simple cases. In the more complex cases, which are of most interest, the conclusions of quantum theory remain locked up in a series of equations whose consequences are quite uncertain.

Mathematicians have devised two methods for solving these equations approximately: the valence bond or resonance method and the method of molecular orbitals. Neither is logically satisfactory since each involves such gross simplifications that its validity can only be estimated empirically. However, both are very successful in practice, and for lack of anything better one must base any chemical theory on one or other of them.

Previous writers in this field have approached chemistry from the standpoint of the resonance method and their general interpretation of chemical phenomena is now well known. This approach is most unsuitable from the organic chemist's point of view since it involves a new symbolism and a novel and uncongenial outlook. (A cursory examination of the literature shows how difficult it is for chemists to distinguish intuitively between resonance and tautomerism.) For these reasons the molecular orbital method has much to offer. It provides a picture of molecular structure closely akin to that of classical organic chemistry; in both, charge migrations, residual affinity, and the like, appear in similar forms. Therefore if the older electronic symbolism is reinterpreted in terms of molecular orbital theory, it can still be used as a valid representation of chemical phenomena. The author has tried to follow this line of approach.

The general purpose of this book has been to give as complete an account as possible of organic chemistry in the light of modern quantum theory; covering all the known types of electronic processes and considering by way of example all the main organic reactions. It was also thought best to discuss the mechanism of each reaction in detail, placing emphasis on the results of recent physico-chemical investigation. This project met with two difficulties.

Firstly, there was the unfortunate rift that exists to-day between physical and organic chemistry. Few chemists have a real knowledge of both subjects—and incidentally fewer still have also a knowledge of quantum theory. Yet a knowledge of all three is essential for a proper understanding of organic chemical theory. The author has tried to meet this difficulty, at least partially, by making the whole treatment non-mathematical and by giving a general account of quantum theory and the necessary physico-chemical principles in some preliminary chapters.

Secondly, so wide a field could not be covered in a book of reasonable size without severe compression. Little space has been given to historical development or questions of priority, no author index has been compiled, and references have been given only for the reader's benefit. The electrostatic theory of reactivity has not been discussed since the author considers it to be mistaken; his reasons will be obvious to the reader. No attempt has been made to indicate specifically the author's responsibility for any novel ideas presented here.

I owe a great debt of gratitude to Professor Sir Robert Robinson on whose unrivalled knowledge of organic chemistry in general, and this field in particular, I have drawn heavily. It is also a pleasure to acknowledge my indebtedness to Professor C. A. Coulson for his guidance in matters connected with quantum theory, and to Dr. C. H. Bamford and Mr. C. E. Phillips who read the book in manuscript and made many helpful suggestions. I wish to thank the officers of the Clarendon Press for their unfailing help and encouragement.

M. J. S. D.

October 1948

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CHAPTER I

THE QUANTUM THEORY OF VALENCY

THE application of the new quantum mechanics of Heisenberg and Schrödinger to chemistry in general, and organic chemistry in particular, has been hampered by two facts. Firstly, the mathematicians and physicists who have devised and elaborated the new theory have naturally had little or no knowledge of chemistry, and they have, moreover, been mainly interested in the quantitative application of the theory in a few simple problems and not in its qualitative application to more complex cases. Secondly, chemists have felt that the new theory must be unintelligible without a more detailed knowledge of mathematics than they possess, and many have also clung to the older ideas of atomic structure because they found them easier to visualize. Some physicists have tried to bridge the gap by presenting chemists with a simplified 'resonance theory' which can be applied to chemical problems with the aid of simple rules and no theoretical knowledge of the underlying principles. This solution could hardly be successful, and in practice even chemists of repute have applied it fallaciously. It is our purpose to show that the ideas underlying quantum theory are actually very simple, and that they can easily be used by non-mathematicians in a qualitative treatment of chemical problems. Combined with the extensive knowledge of electronic processes that organic chemists have independently acquired, this approach gives by far the best general picture of chemical reactions at present available.

The Schrödinger treatment, which has proved the more convenient for most purposes, defines a system of electrons in terms of a function ψ; the value of ψ^2 at any point represents the probability that the electrons will be there.† In fact ψ^2 may be taken as the measure of density of an 'electron gas' representing the average electron distribution over a comparatively long period. It is fundamental in the new theory that this electron distribution represents all we can know about the position of the electrons; to localize them more exactly is impossible. Once ψ for a system is known in terms of the coordinates, it is possible (in principle) to calculate all the physical properties of that system, and therefore the failure to localize the electrons more exactly is of little practical importance.

For a one-electron system in Cartesian coordinates, the Schrödinger equation takes the form

$$\frac{\partial^2\psi}{\partial x^2}+\frac{\partial^2\psi}{\partial y^2}+\frac{\partial^2\psi}{\partial z^2}+\frac{8\pi^2 m}{h^2}(W-E)\psi = 0,$$

where m is the mass of the electron, W the total energy, and E the potential energy. To solve this equation for a given system, the potential energy must first be expressed in terms of the coordinates. Thus in the hydrogen atom, where the potential energy of the electron at a distance r from the nucleus is $-e^2/r$,

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† Strictly the quantity is $\psi\psi^*$, where ψ^* is the complex conjugate of ψ. If ψ is real, $\psi = \psi^*$ and $\psi\psi^* = \psi^2$.

$$E = -\frac{e^2}{r} = -\frac{e^2}{(x^2+y^2+z^2)^{\frac{1}{2}}}.$$

In general, the equation has the peculiar property that it can only be integrated to give a physically possible function for ψ when the total energy of the system, W, has certain definite values; that is, the system can only exist in a series of discrete states, each with a definite energy. In the case of the hydrogen atom these correspond to the states of the Bohr model, and the values of the energy-levels of the atom obtained by the two methods of approach are virtually identical. Substituting any of these values for W in the equation and integrating we can find the corresponding electron-distribution function ψ in terms of known quantities and the coordinates. Quantization is thus introduced in a simple and logical manner as the mathematical condition that the equations should be integrable.

In more complex atoms the ideal procedure would be similar, but in practice mathematical difficulties arise. In a system containing more than one electron the interelectronic repulsion will appear in the potential energy function, and since this involves the position of both electrons it becomes impossible to deal with each separately. The combined equation, moreover, involves not only the complex potential energy function but also six variables instead of three—three coordinates for each electron. In practice the direct integration is impossible with existing techniques and even in helium the energy states must be calculated by numerical methods of successive approximation. Naturally the difficulties become fantastic in more complex atoms and only approximate treatments are feasible.

The simplest of these involves the omission of the terms in the potential energy function which represent interelectronic repulsion. Each electron is then supposed to move independently in the field of the nucleus, its energy-levels and ψ-functions being identical with those of the electron in hydrogen apart from the change of scale due to the increased nuclear charge. This method gives a qualitatively correct picture of the shapes of the electron orbitals,† but the energy-levels so calculated are much too low. The essential point in the treatment is, however, this: by omitting the interelectronic terms we reduce the initial n-electron problem to n one-electron problems which are soluble. A number of refinements have been devised whereby the interelectronic terms can be reintroduced in approximate form without affecting this desirable simplification; in each one-electron problem we reintroduce the other electrons as a smoothed-out distribution of negative charge, so that the field in which our electron moves may be complex but does not vary with time; the integrations then remain possible. The most successful and ingenious of these methods is

† The electron may be thought of as moving in an 'orbital', the average locus over a long period being expressed by the ψ-function.

Hartree's 'method of the self-consistent field'; in it the average electron distributions must be so chosen that each represents the motion of the corresponding electron in the average field of all the others. This field, being a time-average, does not vary with time, and the integrations are therefore feasible.

By these methods important conclusions have been reached. The electrons in an atom fit into a series of discrete orbitals; in the ground state of the atom the electrons occupy the lowest-energy orbitals available. Only two electrons can fit into each orbital, and then only if they have opposite spins; this follows from Pauli's principle that no two electrons can occupy exactly the same energy state. The orbitals form groups, each defined by an integral 'principal quantum number' n; in general the energies of the groups are in order of their principal quantum numbers. The orbitals in a group are distinguished by the 'azimuthal quantum number' l which can have any integral value from 0 to $(n-1)$; states with $l = 0$ are called s-states, with $l = 1$ p-states, $l = 2$ d-states. There are $(2l+1)$ orbitals with quantum numbers n, l; these are distinguished by the 'magnetic quantum number' m, which can have any integral value from $+l$ to $-l$. It will be seen from this brief summary that there are

$$(2n-1)+(2n-3)+...+1$$

orbitals in the group with principal quantum number n; the total number of electrons that can be placed in them is therefore

$$2\{(2n-1)+(2n-3)+...+1\}.$$

In this way the familiar results are obtained that the lowest quantum level $(n = 1)$ holds two electrons; the next $(n = 2)$ holds eight, and so forth; the application of this principle to the periodic table is well known.†

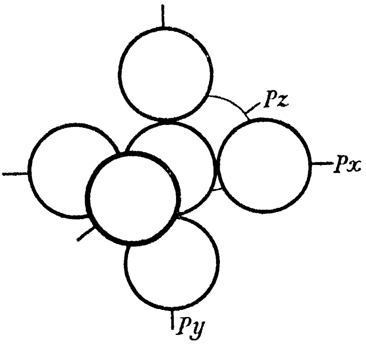

FIG. 1.

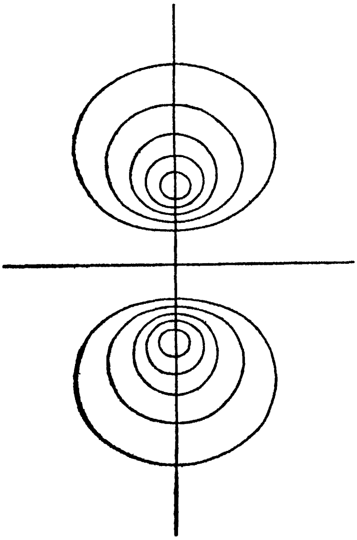

FIG. 2.

The electron distributions in the various states are also important. An s-state is always spherically symmetrical; a p-state has axial symmetry. Fig. 1 (after Pauling) shows diagrammatically the shapes of the 2s and three 2p states in neon where they are all filled. Fig. 2 represents a cross-section of the p_y orbital, the lines representing contours of equal electron-density. The *d*-states are not of much importance in organic chemistry.

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† Cf. N. V. Sidgwick, *The Electronic Theory of Valency*, Clarendon Press, Oxford, 1927.

The electrovalent link can, in principle, be treated by methods already described. Its formation involves the transfer of an electron from one neutral atom or group to another with the production of two ions. The process will be exothermic, i.e. the bond will be stable, if the electron affinity of the second atom or group exceeds the ionization potential of the first, the electron affinity of a group being defined as the energy liberated in its combination with a free electron. The ionization potentials and electron affinities of atoms can be approximated by Hartree's method.

But the covalent link introduces quite new principles. It is formed by the sharing of two electrons between two nuclei, each electron moving in the field of both nuclei. The process could not be satisfactorily explained in the terms of the Bohr atom. The quantum-mechanical treatment is satisfactory in principle, but extremely difficult in practice, since it is a difficult problem to solve even the simple equation for one electron moving in the field of two nuclei, quite apart from the further complications due to interelectronic repulsion in multi-electron molecules. Accurate solutions of the wave equation have been obtained only for the two simplest molecules, H_2 and H_2^+, and the ground-energies and energy-levels so calculated are in exact agreement with those found experimentally. In other cases only very approximate treatments are feasible, but these, though quantitatively of little value, are nevertheless of the greatest significance since they give a clear understanding of the physical basis of chemistry.

It is necessary to simplify the *n*-electron problem by neglecting interelectronic repulsions, thus reducing it to *n* one-electron problems. The further difficulty, that the electric field in which bonding electrons move is not centrally symmetrical, is avoided by expressing the 'molecular orbitals' of these bonding electrons in terms of atomic orbitals. The molecular orbital must resemble an atomic orbital in the vicinity of each nucleus, since the electron is then moving approximately in the field of one nucleus only; so it is reasonable to express the molecular orbital in terms of the two atomic orbitals to which it approximates near the two nuclei.

This type of treatment has been carried out by two different procedures. In the simpler of the two, the Molecular Orbital method (MO for short) of Hund, Mulliken, and others, the molecular orbital of each electron in the molecule is expressed as a linear combination of atomic orbitals, following the argument of the previous paragraph. The total ψ-function (Ψ) for the molecule is a measure of the total electron-distribution, so the value of Ψ^2 at any point is a measure of the probability that all the electrons in the molecule will be there; hence Ψ^2 is written as a product of the ψ^2's for individual electrons, and Ψ as a product of the individual ψ's.

The method may be illustrated by considering an imaginary diatomic molecule AB containing two electrons. When electron 1 is near nucleus A it will move approximately in an A-atom-like orbital, ψ_A^1. Similarly when near B, it will move in a B-atom-like orbital, ψ_B^1. Therefore the molecular orbital may be expressed approximately as $(a\psi_A^I+b\psi_B^I)$, where a, b are constants. The molecular orbital of the second electron may similarly be written as $(a\psi_A^{II}+b\psi_B^{II})$. The Ψ-function for the whole molecule is represented by the product of all the molecular orbitals; in this case we have

$$\begin{aligned}\Psi &= (a\psi_A^I+b\psi_B^I)(a\psi_A^{II}+b\psi_B^{II}) \\ &= a^2\psi_A^I\,\psi_A^{II}+b^2\psi_B^I\,\psi_B^{II}+ab(\psi_A^I\,\psi_B^{II}+\psi_A^{II}\,\psi_B^I).\end{aligned} \tag{1}$$

In this equation the term $a^2\psi_A^I\,\psi_A^{II}$ represents a state in which both the electrons are on the A nucleus, i.e. an ionic state A^-B^+; similarly the term $b^2\psi_B^I\,\psi_B^{II}$ represents an ionic state A^+B^-. The other terms represent a symmetrical non-polar state. Unless $a = b$, one or other ionic form will predominate, and the molecule will have an electric moment; moreover, by varying the coefficients we can express all degrees of polarity between the ionic extremes (in which $a = 0$, $b = 1$, or $a = 1$, $b = 0$). The electrons both fit into one single molecular orbital, with opposite spins (cf. the Pauli principle). This orbital is found to be axially symmetrical so that free rotation about it is possible, and the electron-density is greatest along the line joining the nuclei. The whole picture is a most satisfactory one for a normal single bond; moreover, the accurate treatment of the hydrogen molecule confirms it in detail.

From the Ψ-function of the molecule the energy, and hence the heat of formation, can be calculated. The energy of a single bond between two nuclei may be written as $e_x+e_y+e_{xy}$, where e_x, e_y are the energies of the component atomic orbitals, e_{xy} being the change in total energy due to bond-formation, that is, the *binding energy* of the bond. Bonds can be formed from any pair of orbitals in the two atoms, but if a bond is formed from an orbital of higher energy than that occupied originally by the electron, the net energy liberated in forming the bond will be correspondingly less; hence an atom forms its most stable bonds in general from orbitals of the same principal quantum number as its outermost electrons. Moreover, each atomic orbital can be used to form only one stable molecular orbital. Hence the maximum covalency of an atom should be equal to the number of atomic orbitals in it with principal quantum number equal to that of its outermost electrons. This, of course, corresponds to the earlier qualitative ideas (*vide* Sidgwick). Moreover, it can be shown that the term e_{xy} is numerically greater the greater the overlap in space of the orbitals forming the bond; hence the more the orbitals overlap the greater the binding energy of the bond. Thus a p-orbital (Fig. 2) is axially symmetrical and will overlap most efficiently an atomic orbital on another atom if the second atom lies on that axis; a bond formed by a p-orbital will therefore tend to be directed along the orbital axis since it then has the greatest binding energy.

In forming a bond between two atoms, each must contribute an atomic orbital to form the bonding orbital. The latter will hold two electrons only, according to the Pauli principle, and so the two atomic orbitals must initially hold only two electrons between them if bond-formation is to be possible. Either each atom must have one electron in the orbital which it is about to contribute to the bond, or one atom must have two and the other none. In the former case a normal covalent bond is formed, in the latter a coordinate or dative bond. Thus in the formation of HCl from atoms each atom contributes an orbital with one electron:

$$\mathrm{H}\cdot + \cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}: \rightarrow \mathrm{H}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:$$

but in the formation of trimethylamine oxide from $\mathrm{Me_3N}$ and an O atom the nitrogen contributes both bonding electrons:

$$\mathrm{Me_3N}: + \overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{O}}}: \rightarrow \mathrm{Me_3N}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{O}}}:$$

There is therefore no essential difference between the two types of bond. This point is further emphasized if we regard coordination as taking place by an initial one-electron transfer:

$$\begin{aligned}\mathrm{Me_3N}: + :\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{O}}}: &\rightarrow \mathrm{Me_3}\overset{+}{\mathrm{N}}\cdot + \cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{O}}}:^{-}\\ &\rightarrow \mathrm{Me_3}\overset{+}{\mathrm{N}}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{O}}}:^{-}\end{aligned}$$

This representation shows that the bond is really a single bond formed by $\mathrm{Me_3}\overset{+}{\mathrm{N}}$ and $\overset{-}{\mathrm{O}}$, and hence must be highly polar (p. 37). Such bonds have been represented by arrows, but since we shall use that symbol for another purpose, we shall write coordinate bonds as ionic single bonds, e.g.

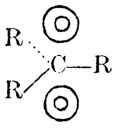
$$\mathrm{Me_3}\overset{+}{\mathrm{N}}\text{—}\overset{-}{\mathrm{O}}.$$

It follows that an atom containing a bonding orbital with only one electron, or no electron, will be very ready to combine chemically with other atoms and so will be chemically unsaturated. (By a bonding orbital we shall always mean an orbital with the same principal quantum number as the outermost electrons in the atom.)

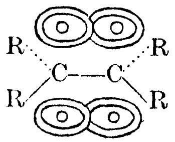
It has so far been assumed that a closed shell of electrons can be expressed in only one way; for instance, that the shell with $n = 2$ contains four orbitals, $2s$, $2p_x$, $2p_y$, and $2p_z$. It is, however, possible to express the shell alternatively as any four linear combinations of these provided that the combinations all add up to the same total $(2s+2p_x+2p_y+2p_z)$ and fulfil certain other mathematical conditions which do not matter here. The new orbitals, a, b, c, d, can then serve as bases for bonds. Now in general these alternative states have higher energies than the 'normal' state, $(2s)(2p)^3$, but the modified orbitals may be so well suited geometrically for bond-formation (i.e. they may be so highly concentrated in one direction that they overlap exceptionally efficiently with other atomic orbitals there) that the molecular orbitals they form may actually have lower energies than those formed from the normal atomic orbitals. Carbon, for example, is normally quadrivalent, having four bonding orbitals ($n = 2$)

available and four electrons in them to form bonds. Carbon could form strong bonds through its three $2p$ orbitals, which are strongly directed in space; but then the fourth bond would be weak, being formed from a spherical $2s$ orbital. Therefore on balance a more stable set of bonds are formed by orbitals which are suitable linear combinations of $2s$ and $2p$ orbitals. The best of these combinations comprises a symmetrical set of four *hybrid*† orbitals, all identical and all strongly bonding, directed tetrahedrally. Quadrivalent carbon should therefore be tetrahedral—as, of course, is known to be the case. Similar arguments show that trivalent boron should be planar, trivalent nitrogen pyramidal, and divalent oxygen and sulphur angular, the ROR and RSR angles being somewhere between 90° and 109°. All these conclusions have been confirmed by detailed physical measurements. Moreover, all these 'σ-bonds' are axially symmetrical like the one in hydrogen; free rotation about them should be possible and all are formed essentially by a shared pair of electrons as the Lewis theory had suggested.

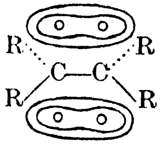
Carbon can also form planar trivalent compounds in which the bonding orbitals, like those of boron, are formed by hybridizing one s and two p orbitals. In carbon there is an odd electron left over, and this occupies the third p-orbital with a node in the plane (I).



(I)



(II)



(III)

Since the odd p-orbital is only half full, the resulting molecule should be highly unsaturated. These conclusions agree most satisfactorily with the known properties of aliphatic radicals like methyl.

If two such trivalent carbons are linked together, however, their odd p-electrons may overlap laterally (II); a new kind of bond, a 'π-bond', can then be formed if the electrons have opposite spins. The electron-distribution in this bond has a node in the plane of the molecule and streamers of electron-density above and below; it is therefore quite unlike an ordinary σ-bond in appearance (III). Obviously the p-orbitals only overlap if they are parallel; therefore the atoms forming it cannot rotate about the π-bond without breaking the bond. Since the π-bond between carbon atoms is strong (heat of formation, 64 Cals.), though not quite as strong as a σ-bond (heat of formation C—C, 81·1 Cals.), the molecule will be rigid. Also the four groups attached to the carbon atoms must lie with them in a plane. These results are in excellent agreement with the known facts about ethylene derivatives; the combination $(\sigma+\pi)$ bond is evidently what the organic chemists have always called a double bond. We now see that it is not really a double bond, i.e. twice a single bond, but something new in kind. The same applies to the triple bond which is really a

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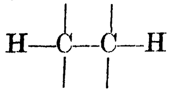
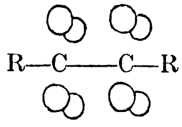
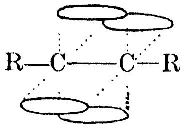
† A hybrid orbital is one formed from a linear combination of atomic orbitals.

$(\sigma+2\pi)$ bond; acetylene, for example, is derived from a linear tetra-radical  $\mathrm{H-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-H}$ in which the bonding orbitals of the carbon atoms are hybrids of an *s* and a *p* orbital in each case; the two odd electrons on each carbon occupy the two other *p*-orbitals with nodes in its axis (IV); if the *p*-orbitals are parallel and the corresponding electrons have opposite spins, two π-bonds at right angles can be formed (V).



(IV)



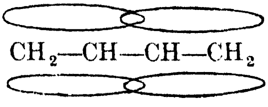
(V)

A quadruple bond is impossible in the absence of a fourth dimension since the orbitals forming it would have to be at right angles to three lines, themselves mutually perpendicular.

Similar σ- and π-bonds can, of course, be formed likewise by other atoms; indeed, in the case of NN bonds the π-bonds are actually the more stable. Thus the heats of formation of N—N and N=N are, respectively, 60 and 152 Cals./mol.

The extra stability acquired by the radical (II) through formation of the π-bond may be explained by an analogy. The new theories do not attach any meaning to the exact position of an electron in an atom or molecule, but represent it rather as a cloud of 'electron gas'; in the diradical each electron is 'concentrated' round one nucleus, but in the ethylene derivative each has 'expanded' to cover two nuclei. The analogy of adiabatic expansion of a gas then suggests that the expanded electrons should have less energy than the concentrated ones.

In ethylene the π-electrons occupy one molecular orbital of lowest energy. In butadiene we might therefore suppose that the four electrons would occupy in pairs two π-orbitals bonding the end pairs of carbon atoms (VI). However, if the whole molecule is planar these orbitals themselves overlap; two more stable orbitals then become available, covering all four carbon atoms; the one with lower energy bonds all four while the higher bonds the end pairs and antibonds† the centre pairs. All are then linked by π-bonds of sorts, but the end pairs are linked more strongly; the formula of butadiene may then be written as (VII).



(VI)

$\mathrm{CH_2\overset{---}{-}CH\overset{\cdots}{-}CH\overset{---}{-}CH_2}$

(VII)

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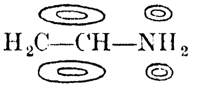
† If an orbital has a node between two atoms it not only does not bond them but actually weakens any bond already existing between them.

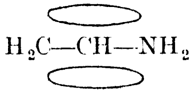
Thiele would say that we had reinvented his partial valency theory! Organic chemists will not quarrel with this representation which was abandoned only because the earlier electronic theory made it appear meaningless.

For this 'conjugation' to be possible, the whole molecule must be planar so that the constituent orbitals can overlap; rotation about the central bond is only possible if we 'compress' the electrons into two ethylenic linkages as in (VI). However, the energy required to do this is small ($\simeq$ 5 Cals.) so that actual *cis-trans* isomerism about the central bond is not observed in butadiene derivatives. The terminal bonds, being much stronger, give rise to normal geometrical isomers.

p-Orbitals can also overlap with π-orbitals to form extended conjugated orbitals. Thus in vinylamine with the nitrogen in a planar sp_2 configuration the unshared electrons in the third p-orbital can overlap with the C=C π-electrons (VIII). Two extended π-orbitals can thus be formed which will hold the two nitrogen electrons and the two C=C π-electrons (IX). If the π-electrons were evenly shared, the nitrogen would then have 4/3 of a π-electron as its share of the whole. Since in the unconjugated system the nitrogen had two p-electrons, it is evident that the conjugation will give the nitrogen a positive charge, and the carbons a negative one. Actually the electrons are not shared evenly so that the effect is much smaller; nitrogen has a much higher electron-affinity than carbon and so acquires more than its share of the π-electrons. Nevertheless, the chemical behaviour of vinylamine derivatives is affected in the expected direction by conjugation. The allyl anion (X) has a similar structure in which the electrons are shared more evenly. These conclusions may be summed up in the statement that n p-orbitals on n adjacent suitably oriented atoms can coalesce to form the whole number $\frac{1}{2}n$ or $\frac{1}{2}(n+1)$ extended π-orbitals of low energy. Thus if n is odd, the extended orbitals will hold $(n+1)$ electrons, and so one atom in such a system can contribute two electrons to the common stock. It is also obvious that the polarization of the π-electrons in vinylamine, due to the high electron-affinity of nitrogen, will make its electronic structure approximate to that of the unconjugated structure (VIII); hence we should expect its extra stability due to conjugation to be less than that of the symmetrical allyl anion (X). In general, the extra stability due to conjugation is greater the more evenly the π-electrons are shared in the conjugated structure.


$H_2C{-}CH{-}NH_2$

(VIII)

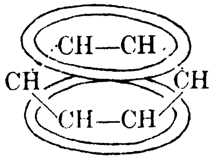

$H_2C{-}CH{-}NH_2$

(IX)

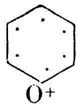
$(CH_2\cdots CH\cdots CH_2)^-$

(X)

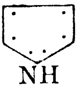
Still more striking is the theoretical treatment of benzene. Here six π-electrons are available for attachment to a planar symmetrical ring of six methine groups. Now it is found† that for electrons moving in the axial field of a symmetrical planar ring, as opposed to the central field of a single nucleus, exactly three low-energy orbitals are available. In benzene these accommodate the six π-electrons; the resulting closed shell of molecular orbitals resembles the closed atomic shells of inert gases, and confers extra stability on the molecule. Following our analogy we may ascribe this extra stability to the fact that the π-electrons in benzene have 'expanded' to cover six nuclei instead of two as in ethylene or a Kekulé structure. The molecular orbitals are symmetrical, forming rings of electron-density above and below the carbon ring (XI), and the symmetry and planarity of the molecule are, moreover, necessary for it to acquire this large extra stability. Organic chemists have long recognized the symmetry of benzene and represented it in various ways; here then is their theoretical justification. It is interesting that the symmetrical π-electron rings are analogous to the electrons in super-conducting metals; benzene is therefore strongly diamagnetic, just like a ring of super-conducting lead.



(XI)



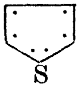
(XII)



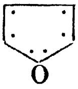
(XIII)

The rings of pyridine, pyrimidine, etc., are exactly similar, the hetero-atoms each contributing one electron to the common stock. The same is true of the pyrylium salts (XII).

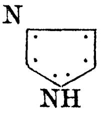
In pyrrole (XIII) there are only five atoms in the ring; however, the nitrogen can now contribute *both* its free electrons so that again all three orbitals are filled. The NH group thereby acquires a partial positive charge and so acidity; the methines acquire partial negative charges and thereby enhanced reactivity to cationoid reagents. Similar considerations apply to thiophene (XIV), furane (XV), and the other aromatic five-membered heterocycles like iminazole (XVI). (The dots represent π-electrons.)



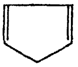
(XIV)



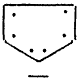
(XV)



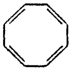
(XVI)



(XVII)



(XVIII)



(XIX)

Cyclopentadiene (XVII) by losing a proton can give the anion (XVIII) which again has the requisite symmetry and six π-electrons; the anion (XVIII) is thus greatly stabilized with respect to (XVII)—i.e. the acidity of (XVII) is greatly increased. Cyclopentadiene reacts with alkali metals to form salts and is certainly enormously more acidic than paraffin hydrocarbons.

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† Hückel, *Z. Elektrochem.* 1937, **43**, 752, 827.

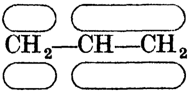
There is, of course, no qualitative difference between aromatic compounds and open-chain polyenes; but closing up the mesomeric system into a ring leads to a great increase in resonance energy. The six π-electrons in benzene resemble qualitatively the four in butadiene, but benzene is more degenerate and has the higher resonance energy.

In these symmetrical ring-compounds there is one orbital of lowest energy and then a degenerate level of two equal-energy orbitals. Thus in cyclobutadiene, with four π-electrons, two must occupy the degenerate level and, according to empirical rules laid down by spectroscopists, they should occupy separate orbitals with parallel spins. Thus cyclobutadiene should contain two unpaired electrons and so be a diradical; the failure to prepare it is not surprising.

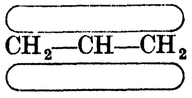
Cyclo-octatetraene (XIX) is not aromatic, being highly unsaturated,[†] and having a low resonance energy (p. 34) and a puckered ring.[‡] If it were aromatic, the carbon atoms in the ring would be sp_2 hybridized and the undistorted valency angles of sp_2 hybridized carbon is 120°. In planar cyclo-octatetraene the annular valency angles would be 130°; evidently the strain so produced would be greater than the resonance energy gained by assuming a planar aromatic structure.

Bamberger fifty years ago pointed out that the aromatic character seemed to depend on the presence in a 5- or 6-membered ring of six dormant valencies; this idea, first put into electronic terms by Kaufmann,[§] was later stressed by Robinson[||] in his theory of the 'Aromatic Sextet', as he termed this six-electron group; the idea has now been shown to rest on a quantum-mechanical basis.

Trivalent carbon is highly unsaturated; it can be stabilized greatly by attachment to double bonds. Thus in the allyl radical the odd p-electron overlaps with the two π-electrons of the double bond (XX); if the whole radical is planar, the three electrons can be fitted into two orbitals of low energy covering all the atoms; the lower orbital is filled, but the higher is not, so that the compound is still unsaturated; it is, however, much more stable than free methyl for the same reason that the conjugated form of butadiene is more stable that the unconjugated. The resulting allyl radical is completely symmetrical (XXI).



(XX)



(XXI)

Further conjugation may still further stabilize a radical; the extreme case is seen in the triarylmethyls, some of which are quite stable and show no tendency to dimerize. Similar radicals are also formed by other elements (Chapter XII).

[†] Willstätter and Waser, *Ber.* 1911, **44**, 3442; Willstätter and Heidelberger, ibid. 1913, **46**, 518; Reppe, *Modern Plastics*, 1946, **23**, 169, 218, 220.

[‡] Lippincott and Lord, *J.A.C.S.* 1946, **68**, 1868.

[§] *Die Valenzlehre*, 1908.

[||] 4th *Solvay Report*, 1931.

It is clear from this discussion that a π-bond is a very variable quantity; π-electrons are much more mobile than the electrons in σ-bonds which are relatively fixed. Thus two π-electrons form one π-bond in ethylene, two π-bonds in benzene, and three in graphite. The central bond in butadiene is a very weak π-bond; the terminal π-bonds, however, are strong. It is easy to understand the difficulties which classical bond theory encountered in the case of these unsaturated compounds and which led Thiele to propound his theory of partial valencies. This theory can now be stated in more quantitative terms by the definition of 'bond orders', the order of a bond being anything between one and three. Thus the orders of bonds in ethylene, acetylene, benzene, and graphite are respectively 2, 3, 1·5, and 1·33. Since the length of a bond is found to vary with its order, it is possible to measure the order of a bond by determining its length. Fig. 3 shows the relation between length and order† for CC bonds.

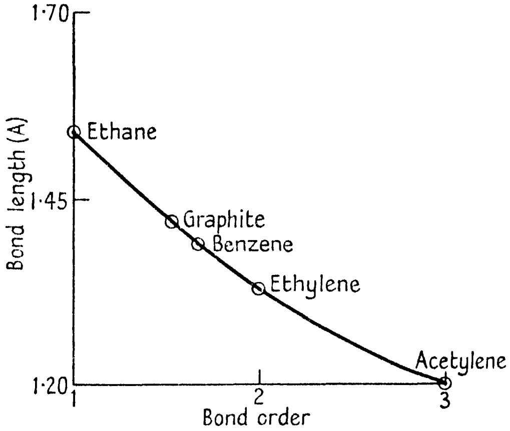


FIG. 3.

The existence of molecules in intermediate states between different classical structures was discussed by Ingold in terms of the earlier electronic theory; his term 'mesomerism' for the phenomenon is a happy one and has been generally accepted. Even in cases of almost complete degeneracy,‡ however, classical bond-structures can generally be used if it is remembered that the symbol C═C in conjugated systems represents not a double bond but a 'more double' bond and C—C a 'more single' bond; for the chemical reactivity of such systems is determined by the position of the bonds with the highest order. Even a small difference in bond order may make a very large difference to the rate of reaction of an unsaturated system, since the bond order will affect the activation energy of the reaction, thus involving an exponential term in the equation for the velocity constant (*vide* Chapter II). The reactions of naphthalene are well represented by the Erlenmayer formula (XXII), although the absolute difference between the 1:2 and 2:3 bonds is quite small.

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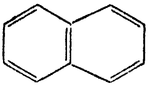
† The orders are those calculated by Coulson, *Proc. Roy. Soc.* 1939, A **169**, 413.

‡ A molecule is said to be 'degenerate' to the extent that its classical bond-structure fails to express its actual state.



(XXII)

We will now consider an alternative approach to the problem of chemical combination, the valence-bond method first devised by Heitler and London and later extended by Slater, Pauling, Hückel, and others. In this a bond between two atoms is supposed to be formed by the pairing of two electrons with opposite spins, one on each atom. The argument is as follows: if we consider two atoms A, B, each with an odd electron, we can write the Ψ-function for the system as

$$\Psi_1 = a\psi_A^{I}\,\psi_B^{II}.$$

Now suppose that the electrons on the atoms exchange places; the new Ψ-function will be

$$\Psi_2 = a\psi_A^{II}\,\psi_B^{I}.$$

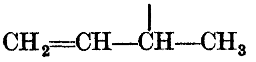
But when the atoms are close together, these two states will be indistinguishable, because we have no way of telling electrons apart; all electrons are identical. Therefore all we can hope to say is that the system will have a probability of being in one state or the other. Since the electrons are identical, the one state must be as likely as the other, for symmetry; therefore the Ψ-function for the system should be written as the sum† of the two functions Ψ_1, Ψ_2; i.e.

$$\Psi_{VB} = a(\psi_A^{I}\,\psi_B^{II}+\psi_A^{II}\,\psi_B^{I}).$$

Calculation shows that the resulting electron-distribution is axially symmetrical and that the electrons are concentrated between the two nuclei; the bond is also symmetrical and non-polar.

This is in fact a very good quantum-mechanical picture of a classical single bond.

Now suppose we have a more complicated molecule in which two or more classical bond-structures are possible; for example, the α-methylallyl radical where the two structures (M) and (N) are equally reasonable.



$CH_2{=}CH{-}\overset{|}{C}H{-}CH_3$

(M)

$-CH_2{-}CH{=}CH{-}CH_3$

(N)

Suppose that the valence-bond (VB for short) function for the first is ψ_M and for the second ψ_N; then since the position of the nuclei in the two forms is much the same and since they therefore differ only in electron-distribution, the same argument as before shows that we cannot tell them apart. We can only hope to know the probability that the system at any moment is in one state or the other. These probabilities need not be the same since the states are not identical; therefore the 'true' electron-distribution will be represented by a linear combination of the two functions ψ_M, ψ_N, thus:

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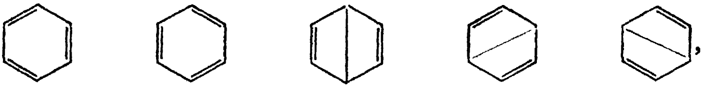
† A numerical factor must be introduced so that the total probability of the electron being somewhere in space is unity. This factor is called a 'normalizing factor'.

$$\Psi = m\psi_M + n\psi_N.$$

In order to find the values of the coefficients m, n we make use of the following argument. The actual electronic configuration of the molecule must be such that its energy is as low as possible; therefore any approximate ψ-function must represent a higher energy state. For if some ψ-function existed which would give the molecule a lower energy, the molecule would adopt it, and it would become the true function for the molecule. The closer an approximate ψ-function is to the true one, the nearer its equivalent energy will be to the true energy; therefore of two approximate ψ-functions, the one with the lower energy will be the closer to the truth. In our molecule AB we must then adjust the coefficients m, n to make the energy a minimum.

If the two states M, N in such a case differ greatly in energy, it is found that the more stable one is much closer to the true state of the system—as one would expect. In that case one coefficient m or n will be approximately zero, and the molecule will be satisfactorily represented by a single classical bond-structure. If, however, the energies of the two states are comparable, as in our actual example, m and n will be comparable; neither classical structure will then represent the molecule satisfactorily. It will occupy an intermediate state between the component structures and be more stable than either. In that case the molecule is said to be a hybrid of the two structures, or to resonate between them. The extra stability compared with the more stable component structure ('canonical form') is called the resonance energy.

By an extension of the same argument a molecule may be considered as a hybrid of any number of canonical forms; thus benzene is regarded as a hybrid of two Kekulé and three Dewar forms,



the former predominating.

In this system a double bond *is* a double bond, being formed by the pairing of four electrons, two on each atom, in two pairs with opposite spins. A triple bond similarly involves pairing of six electrons, three on each atom triply linked.

For resonance between two classical bond-structures to be appreciable, it is necessary that they should involve almost identical positions for the nuclei (so that they differ only in electron-distribution), their energies must be comparable, and the total number of electrons and the number of pairs of electrons with opposite spins must be the same in both. If these conditions are fulfilled, the theory states that resonance not only can, but must occur.

For quantitative calculation the VB method is more difficult to apply than is the MO (molecular orbital) treatment, but the qualitative rules just given allow a semi-empirical discussion of chemical phenomena which has been brilliantly conducted by Pauling, Wheland, and others (*vide* Bibliography). It has also found great favour with many chemists since the rules of the game are so simple that it can be played happily by almost anyone without any knowledge of the underlying principles involved.

There is actually a simple relation between these two apparently dissimilar methods of approximation. Returning to the fundamental equations for our hypothetical molecule AB:

$$\begin{aligned}\Psi_{\mathrm{MO}} &= a^2\psi_{\mathrm{A}}^{\mathrm{I}}\psi_{\mathrm{A}}^{\mathrm{II}}+b^2\psi_{\mathrm{B}}^{\mathrm{I}}\psi_{\mathrm{B}}^{\mathrm{II}}+ab(\psi_{\mathrm{A}}^{\mathrm{I}}\psi_{\mathrm{B}}^{\mathrm{II}}+\psi_{\mathrm{A}}^{\mathrm{II}}\psi_{\mathrm{B}}^{\mathrm{I}}),\\ \Psi_{\mathrm{VB}} &= c(\psi_{\mathrm{A}}^{\mathrm{I}}\psi_{\mathrm{B}}^{\mathrm{II}}+\psi_{\mathrm{A}}^{\mathrm{II}}\psi_{\mathrm{B}}^{\mathrm{I}}),\end{aligned}$$

the relation is immediately obvious. The VB treatment simply omits the ionic terms. Now the main fault of the MO method is the excessive weight it gives to the ionic terms; this is because in the actual molecule ionic forms are repressed by the mutual repulsion of the bond electrons which tends to keep the electrons on opposite atoms, and it is just these interelectronic repulsions that are ignored in the MO treatment. The VB method, by omitting the ionic terms altogether, greatly over-emphasizes these repulsions; in practice it is found to be an equally good, but not a superior, approximation to the truth. It is extremely satisfactory that the two methods of approximation lead to qualitatively identical results in most cases, although they approach the goal from opposite directions; our confidence in their validity is thus greatly strengthened.

The question of resonance between different canonical forms remains to be cleared up. This may be elucidated by consideration of an imaginary resonating ion $(\mathrm{ABC})^+$ containing two electrons; i.e. a hybrid of (X), (Y), and (Z) according to resonance theory. (The known H_3^+ ion would be an example.)

$$\underset{(\mathrm{X})}{\mathrm{A{-}B\quad C^+}}\qquad\qquad \underset{(\mathrm{Y})}{\mathrm{A^+\quad B{-}C}}\qquad\qquad \underset{(\mathrm{Z})}{\overparen{\mathrm{A\quad B^+\quad C}}}$$

In the MO treatment the molecular orbital of each electron is written as a linear function of three atomic orbitals and the Ψ-function of the molecule is the product of the two molecular orbital functions. Thus:

$$\begin{aligned}\Psi_{\mathrm{MO}} &= (a\psi_{\mathrm{A}}^{\mathrm{I}}+b\psi_{\mathrm{B}}^{\mathrm{I}}+c\psi_{\mathrm{C}}^{\mathrm{I}})(a\psi_{\mathrm{A}}^{\mathrm{II}}+b\psi_{\mathrm{B}}^{\mathrm{II}}+c\psi_{\mathrm{C}}^{\mathrm{II}})\\ &= a^2\psi_{\mathrm{A}}^{\mathrm{I}}\psi_{\mathrm{A}}^{\mathrm{II}}+b^2\psi_{\mathrm{B}}^{\mathrm{I}}\psi_{\mathrm{B}}^{\mathrm{II}}+c^2\psi_{\mathrm{C}}^{\mathrm{I}}\psi_{\mathrm{C}}^{\mathrm{II}}+ab(\psi_{\mathrm{A}}^{\mathrm{I}}\psi_{\mathrm{B}}^{\mathrm{II}}+\psi_{\mathrm{A}}^{\mathrm{II}}\psi_{\mathrm{B}}^{\mathrm{I}})+\\ &\qquad +bc(\psi_{\mathrm{B}}^{\mathrm{I}}\psi_{\mathrm{C}}^{\mathrm{II}}+\psi_{\mathrm{B}}^{\mathrm{II}}\psi_{\mathrm{C}}^{\mathrm{I}})+ca(\psi_{\mathrm{C}}^{\mathrm{I}}\psi_{\mathrm{A}}^{\mathrm{II}}+\psi_{\mathrm{C}}^{\mathrm{II}}\psi_{\mathrm{A}}^{\mathrm{I}}).\end{aligned}$$

In the VB treatment the three individual structures are given by

$$\psi_X = \psi_A^I \psi_B^{II} + \psi_A^{II} \psi_B^I,$$
$$\psi_Y = \psi_B^I \psi_C^{II} + \psi_B^{II} \psi_C^I,$$
$$\psi_Z = \psi_C^I \psi_A^{II} + \psi_C^{II} \psi_A^I.$$

Therefore the total Ψ-function for the molecule is given by

$$\Psi_{VB} = x(\psi_A^I \psi_B^{II} + \psi_A^{II} \psi_B^I) + y(\psi_B^I \psi_C^{II} + \psi_B^{II} \psi_C^I) + z(\psi_C^I \psi_A^{II} + \psi_C^{II} \psi_A^I).$$

Comparing these equations, we see that Ψ_{MO} and Ψ_{VB} differ only by the three terms $a^2\psi_A^I \psi_A^{II}$, $b^2\psi_B^I \psi_B^{II}$, $c^2\psi_C^I \psi_C^{II}$ which the VB treatment omits. Now these terms represent states in which both electrons are on the same atom, i.e. the three ionic states (P), (Q), and (R).

$$\underset{(P)}{A^- \quad B^+ \quad C^+} \qquad \underset{(Q)}{A^+ \quad B^- \quad C^+} \qquad \underset{(R)}{A^+ \quad B^+ \quad C^-}$$

Thus we could if we liked say that the MO treatment represents the molecule as a hybrid of the six states (X), (Y), (Z), (P), (Q), and (R), while the VB treatment represents it as a hybrid of the first three only. In all cases the treatments differ only in that MO over-emphasizes, VB neglects, ionic forms.

Alternatively we may say that the MO and VB methods both try to solve approximately the fundamental problem, that is, to determine the orbitals of all the electrons in the molecule moving in the field of all the nuclei and repelling each other according to the Coulomb law. Since multibody problems are difficult to solve, the effect of the polynuclear field is approximated by writing molecular orbitals as linear expressions of atomic orbitals; this, it must be remembered, is an arbitrary approximation justified only by results.† The interelectronic terms raise even greater difficulties; in the MO treatment they are therefore ignored. As a result the MO treatment gives too much weight to terms representing ionic forms; the VB treatment seeks therefore to remedy this defect by arbitrarily omitting the ionic terms altogether. In practice it is found that the errors introduced by both methods are about equally great.

It may occur to the reader that a better approximation could be obtained by including the ionic terms with arbitrary coefficients so that their contributions to the whole sum could be adjusted. This is of course true, but the mathematical difficulties are usually quite prohibitive. Such a treatment has proved feasible only in the case of hydrogen. It may be added that even then we should have no accurate representation of the molecule; the utmost refinements in the MO and VB treatments of hydrogen gave values for the energy which differed considerably from experiment. The errors introduced by writing molecular orbitals as functions of atomic orbitals are in fact very considerable. It is on this method of approximation that the resonance theory depends. In the more accurate treatment of the hydrogen molecule by James and Coolidge, no terms in the wave-function can be identified with individual classical bond-structures, and the same would undoubtedly be true of other molecules if accurate treatments were possible. The resonance theory can at best be a temporary substitute until such accurate methods are devised.

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† It depends on the theorem that any function can be approximated as a linear combination of arbitrary functions, the closeness of the approximation depending on the skill with which the arbitrary functions are chosen. It happens that molecular orbitals can be approximated quite well in terms of atomic orbitals since both represent similar kinds of phenomena.

The resonance theory suffers from two further defects, admittedly not constitutional but none the less real. First, in spite of all warnings, many organic chemists will continue to regard the various resonance forms in a hybrid as having some kind of real existence; that is, they regard the hybrid as a kind of tautomeric mixture of the forms. This is entirely incorrect. The forms are mere mathematical fictions, and there is no reason why the hybrid should show reactions expected for all, or indeed any, of its forms.

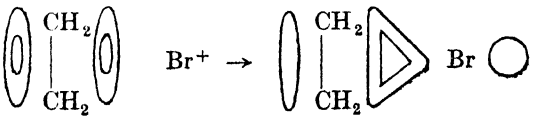
Secondly, it is not always possible to tell which of the possible classical structures for a compound will contribute significantly to the hybrid, since their energies are not always simply estimated. This applies particularly to ionic resonance of the type met in pyrrole and its analogues. The attempt to correlate stability with the number of classical structures possible is also erroneous and misleading, and, moreover, the resonance theory does not emphasize sufficiently the difference in kind between σ- and π-orbitals, nor the special stereochemical relations of the latter.

In any case, resonance notation is cumbersome and tends to obscure the general features of a molecule behind a fog of formulae. All in all, it is a most unsatisfactory rule-of-thumb substitute for a proper understanding of basic principles. It is preferable in every way to use partial valency notation for mesomeric structures since these are rarely ambiguous and never actively misleading. This plan has been followed throughout, except in one or two isolated places where resonance notation happens to be clearer.

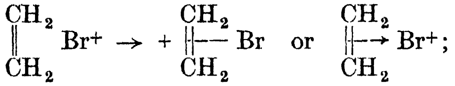
NOTES

1. *The molecular bond*

The formation of a bond between two atoms requires that they should each have an available bonding orbital and that they should possess two electrons between them in those orbitals. Now examination of Fig. 2 and (III) will show that the π-orbital of ethylene resembles closely the p-orbital of a separate atom. There seems to be no reason why the π-orbital should not be able to overlap and coalesce with an atomic orbital of a third atom to give a special kind of molecular orbital covering all three nuclei. The latter orbital will, of course, hold two electrons only, and so bond-formation between ethylene and another atom will only occur if the latter has a vacant bonding orbital. The resulting bond will therefore be of coordinate type, the ethylene acting as the donor. Thus the reaction of ethylene with a bromine cation may be represented (cf. p. 143):



or



$$\begin{matrix}CH_2\\ \|\\ CH_2\end{matrix}\ Br^+ \rightarrow +\begin{matrix}CH_2\\ \|\!\!-\!\!-\\ CH_2\end{matrix}Br \quad\text{or}\quad \begin{matrix}CH_2\\ \|\!\!\rightarrow\\ CH_2\end{matrix}Br^+;$$

cf. $R_3N + O \rightarrow R_3\overset{+}{N}\text{—}\overset{-}{O} \quad\text{or}\quad R_3N\rightarrow O.$

Since the formation of such a dative bond virtually involves transfer of one electron from ethylene to Br^+, it will be facilitated by the relatively low ionization potential of the π-electrons in ethylene.

A similar argument will show that two π-orbitals should be able to overlap to form a bond provided that one of them initially contains no electrons, or that each contains one electron only. Such bonds, one or both components of which is a π-electron-containing molecule, may be termed *molecular bonds*. Their existence was first suggested to explain the mechanism of the benzidine rearrangement,† and much evidence for them will be found throughout the book. It may be added that the π-orbitals of aromatic compounds apparently can also form molecular bonds. Compounds containing molecular bonds have been termed *π-complexes*.

2. *Oxygen and ozone*

A particularly interesting feature of the quantum theory is the explanation it gives for the reactivity of oxygen. In nitrogen (N_2) the electrons fit exactly into a set of atomic and molecular orbitals of minimum energy. The next level consists of two equal-energy π-orbitals, capable of holding four electrons; in fluorine (F_2) these are just filled. In oxygen (O_2), however, there are only two electrons available in this level. The arguments applied to butadiene (p. 11) show that these electrons should occupy separate orbitals with parallel spins; the molecule should then be paramagnetic and have the properties of a free radical. Such is in fact the case.

Oxygen can exist in three low-energy states. In the state of lowest energy, the atoms are linked by a single bond and two one-electron π-bonds; the second state differs from the first in that the odd electrons have antiparallel spins, and the third in that the electrons occupy one π-orbital with antiparallel spins, leaving the other empty. The three states may be written (dotted lines implying one-electron π-bonds, and arrows indicating the spins of the outermost electrons)

$$\underset{^3\Sigma}{O\overset{\cdots}{\underset{\cdots}{—}}O\ (\uparrow\uparrow)} \qquad \underset{^1\Delta}{O\overset{\cdots}{\underset{\cdots}{—}}O\ (\uparrow\downarrow)} \qquad \underset{^1\Sigma}{O{=}O\ (\uparrow\downarrow)}$$

The lowest state (^3P) of the oxygen atom also contains two electrons in separate p-orbitals with parallel spins. ^3P O and $^3\Sigma$ O_2 therefore resemble one another in having two odd electrons in p- or π-orbitals at right angles. It is reasonable that one p-orbital of the former and one π-orbital of the latter should be able to overlap to form a molecular bond. Further, the other p-orbital and the other π-orbital should then be able to overlap laterally to form a π-type molecular bond:

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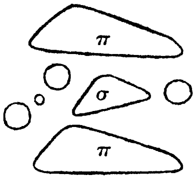
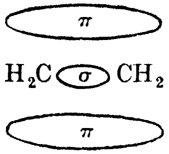
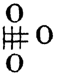
† Dewar, *Nature*, 1945, **176**, 784; *J.C.S.* 1946, **406**, 777.



cf.



According to this theory, ozone should be regarded as a π-complex containing a double molecular bond.



$$\overset{O}{\underset{O}{\#}}\,O$$

If so, the original O_2 atoms should be triply linked in ozone, and therefore about 1·10 A apart, while the other oxygen, held by molecular bonds should be further separated. Recent infra-red spectrum analysis† strongly supports this structure.

3. *Hyperconjugation*

Although σ-orbitals cannot overlap efficiently with adjacent orbitals to form extended orbitals, they can do so to some extent. Thus in ethane the six C—H bonds are formed from hybrid sp_3-orbitals, and the p-components of these can overlap to some extent, forming weak π-bonds between the carbon atoms. The C—C bond in ethane is therefore not a pure σ-bond; it is shorter and stronger than it would be if no conjugation was taking place. This general effect, the conjugation of σ-orbitals, is called *hyperconjugation*. It is mainly confined to hydrogen bonds, and may be related to the very small radius of hydrogen; thus the C—H molecular orbitals differ little in shape and size from carbon atomic orbitals.

The effect is greater when the σ-orbitals overlap with π-orbitals (first-order hyperconjugation) than when they overlap with other σ-orbitals (second-order hyperconjugation). Thus in propene there is considerable hyperconjugation between the methyl and double bond, as is clearly shown by the difference in heat of hydrogenation between propene and ethylene (p. 35). Much physical evidence for hyperconjugation will be found in Chapter III.

4. *The hydrogen bond*

The association of water was ascribed by Sidgwick (ref. p. 3) to coordination, since it was then supposed that the maximum covalency of hydrogen was two. Sidgwick gives numerous other examples of 'coordination' of hydrogen, and this formation of such *hydrogen bonds* is now generally accepted. However, they cannot, as Sidgwick then supposed, be due to coordination, since it is now known that the maximum covalency of hydrogen is one. Moreover, the heats of formation of hydrogen bonds are much less than those of primary valencies, never exceeding 10 Cals. Two explanations have been put forward. According to the first, the phenomenon is due to a special kind of resonance, e.g. in the hydrogen-bonded dimers of carboxylic acids:

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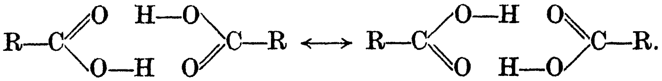
† Adel and Dennison, *J. Chem. Phys.* 1946, **14**, 379. Dewar (*J.C.S.*, 1948) gives a more detailed analysis of the electronic structure of ozone.



This explanation does not account for the failure of atoms other than hydrogen to show the effect, nor for the lack of symmetry of the carboxylic acid dimers (in which the C—O bonds have very different lengths, close to those of the corresponding bonds in esters).

The other explanation, which is now fairly generally accepted, is that the 'hydrogen bond' merely represents an unusually strong charge-dipole attraction. The O—H bond is highly polar, and the small radius of hydrogen allows negatively charged atoms to approach closely, so that they are held very strongly by electrostatic attraction. The O—H bond can hold only one atom in this way because the hydrogen atom is so small that when a negative atom is held on the side opposite to oxygen there is no room for a third atom to approach. Moreover, the attraction of a dipole for a charge is strong only along its axis, so that the electrostatic 'bond' between a charge and a dipole is strongly localized along the axis of the latter.

Hydrogen bonding is most marked with ROH and HF, less with R_2NH or RSH, and very small with R_3CH, since the dipole moments fall in that series. It is particularly interesting that chloroform, where the C—H dipole moment is greatly increased by induction by the polar C—Cl bonds, shows a definite tendency to form hydrogen bonds.

It may be added that hydrogen bonds cannot be distinguished qualitatively from true bonds, for the essence of both is a distortion of atomic or molecular orbitals and a consequent increase in molecular stability. In this sense all four types of bond (σ, π, molecular, and hydrogen) are essentially similar.

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CHAPTER II

CHEMICAL KINETICS, AND THE QUANTUM THEORY OF REACTIONS[†]

According to the law of mass action, the rate of a simple chemical reaction is proportional to the active masses or concentrations of the reactants. The rate can then be expressed as the product of the concentrations of the reactants and of a 'velocity constant' characteristic of the reaction. It is usual to classify reactions according to the number of concentration terms in the product. The rates of first-order reactions vary as the concentration of one reactant, of second-order reactions as the product of two reactant concentrations, of third-order reactions as the product of three reactants, and so forth. If a reaction involves two molecules of one reactant, the concentration will occur twice over in the rate expression, that is, the rate will vary as the square of its concentration. Or to take the most general case, the rate of a reaction

$$aA+bB+cC+...+nN \rightarrow \text{products}$$

will be

$$k[A]^a[B]^b[C]^c...[N]^n.$$

For example, the conversion of *cis*-butene-2 into *trans*-butene-2 at high temperatures is first-order, the rate being proportional to the concentration of butene; the hydrolysis of methyl iodide by sodium hydroxide in aqueous alcohol is second-order, the rate being $k[\text{MeI}][\text{OH}^-]$; and the thermal decomposition of hydrogen iodide is also second-order, the rate being $k[\text{HI}]^2$.

Not all chemical reactions are simple. Many take place in two or more successive stages. In such cases the rate of each stage will be given by the general type of rate-law, but the overall rate of the whole reaction may not. Conversely, a failure to obey the rate-law indicates that a reaction is taking place in two or more stages. If the detailed mechanism is known, it is possible to calculate the relation between the overall rate and the concentrations of the reactants.

The normal procedure (the stationary state method) is to assume that the concentrations of the intermediates in the reaction vary slowly, so that their rates of formation and removal can be equated. The method is best illustrated by a simple reaction $A+B+C \rightarrow$ products; which takes place by the reversible formation of an intermediate D from A and B, followed by reaction of D with C to give the final products. The various reactions are:

$$
\begin{array}{lll}
(1) & A+B \rightarrow D & \text{rate } k_1[A][B] \\
(2) & D \rightarrow A+B & \quad ,, \; k_2[D] \\
(3) & C+D \rightarrow \text{products} & \quad ,, \; k_3[C][D].
\end{array}
$$

[†] A detailed account has been given by Glasstone, Laidler, and Eyring, *The Theory of Rate-Processes*, McGraw-Hill, 1941.

The rate of formation of D is $k_1[A][B]$; its rate of removal is

$$k_2[D]+k_3[C][D].$$

Equating the two we have

$$[D] = \frac{k_1[A][B]}{k_2+k_3[C]}.$$

The overall rate of reaction is then

$$\frac{d[\text{products}]}{dt} = k_3[C][D] = \frac{k_1 k_3[A][B][C]}{k_2+k_3[C]}.$$

If reactions (2) and (3) take place at very different rates, the expression can be simplified. If $k_2 \ll k_3[C]$, the first term in the denominator can be neglected, and the rate approximates to

$$\frac{k_1 k_3[A][B][C]}{k_3[C]} = k_1[A][B].$$

The physical meaning of this result is that almost every molecule of D formed reacts with C to give the product; therefore the overall rate of reaction is determined only by the rate of formation of D, that is, by reaction (1). In such a case the overall rate is equal to that of a 'rate-determining step'. If, on the other hand, $k_2 \gg k_3[C]$, the expression for the total rate becomes similarly

$$\frac{k_1 k_3}{k_2}[A][B][C].$$

Here the concentration of D is essentially determined by the equilibrium represented by equations (1) and (2); its concentration is therefore given approximately by

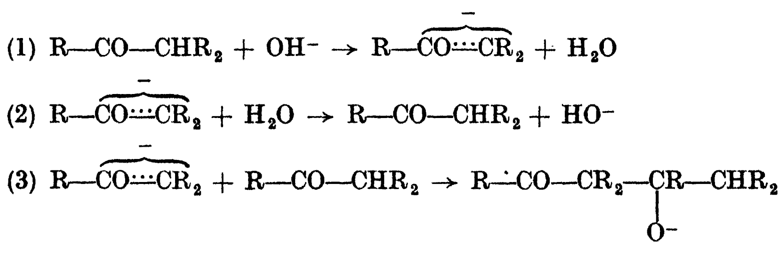
$$[D] = \frac{k_1[A][B]}{k_2}$$

and the overall rate of reaction is $K_3[C]$ times greater. Finally, if $K_2 \sim K_3[C]$, the rate will not vary according to any simple power of [C], but for small ranges may be approximately represented by a relation of the form

$$K[A][B][C]^{\alpha},$$

where $0 < \alpha < 1$.

We may add that the aldol condensation of carbonyl compounds follows this kinetic scheme. The reactions of a carbonyl compound $RCOCHR_2$ are



$$\text{(1) } R\text{—}CO\text{—}CHR_2 + OH^- \rightarrow R\text{—}\overset{-}{\overbrace{CO\cdots CR_2}} + H_2O$$

$$\text{(2) } R\text{—}\overset{-}{\overbrace{CO\cdots CR_2}} + H_2O \rightarrow R\text{—}CO\text{—}CHR_2 + HO^-$$

$$\text{(3) } R\text{—}\overset{-}{\overbrace{CO\cdots CR_2}} + R\text{—}CO\text{—}CHR_2 \rightarrow R\text{—}CO\text{—}CR_2\text{—}\underset{\substack{|\\ O^-}}{C}R\text{—}CHR_2$$

which is of the same form as our simple scheme with A = C = carbonyl compound, D its conjugate anion, and B = OH^-. The extra term $[H_2O]$ in (2) is irrelevant since in aqueous solution the concentration of water is effectively constant. The overall rate is then

$$\frac{k_1[OH^-][RCOCHR_2]^2}{k_2+k_3[RCOCHR_2]}.$$

Chemical equilibrium

If a chemical reaction is reversible, it will lead eventually to a state of equilibrium in which the rates of the forward and backward reactions are equal, so that the net concentrations of the various chemical species in the system do not vary with time.

If we represent the forward and backward reactions as

$$A_1+B_1+C_1+\ldots \rightarrow A_2+B_2+C_2+\ldots$$
$$A_2+B_2+C_2+\ldots \rightarrow A_1+B_1+C_1+\ldots$$

their rates will be given by

$$-\frac{d[A_1]}{dt} = -\frac{d[B_1]}{dt} = -\frac{d[C_1]}{dt} = \ldots = k_1[A_1][B_1][\ldots]$$
$$-\frac{d[A_2]}{dt} = -\frac{d[B_2]}{dt} = -\frac{d[C_2]}{dt} = k_2[A_2][B_2][\ldots].$$

Equating the rates, we have

$$\frac{[A_1][B_1][C_1][\ldots]}{[A_2][B_2][C_2][\ldots]} = \frac{k_2}{k_1} = K,$$

where K is the *equilibrium constant* for the reaction. The equilibrium constant is equal to the ratio of the velocity constants of the forward and backward reactions.

A simple example is the dissociation of hexaphenylethane to triphenylmethyl. The two reactions are

$$C_2Ph_6 \rightarrow 2CPh_3\cdot$$
$$2CPh_3\cdot \rightarrow C_2Ph_6.$$

Their rates are given by

$$k_1[C_2Ph_6] \quad \text{and} \quad k_2[CPh_3\cdot]^2.$$

Hence at equilibrium the concentrations of hexaphenylethane and triphenylmethyl must obey the relation

$$\frac{[C_2Ph_6]}{[CPh_3\cdot]^2} = \text{constant}.$$

Collision theory†

The first successful interpretation of reaction kinetics was based on the very reasonable idea that molecules must collide in order to react. The rate should then depend on the frequency with which the necessary collisions occur, and for bimolecular† reactions at any rate this can be calculated fairly satisfactorily by kinetic theory. It is found, however, that the rates of such reactions are generally very much smaller than would be expected if every collision led to reaction. There are two simple reasons why collisions should be ineffective: the molecules may have to collide with an appropriate orientation, or they may need a certain amount of energy for reaction to occur. The first effect will introduce a 'steric factor', independent of temperature, into the rate expression, while the second will introduce a temperature-variable factor since molecules contain more energy on average at higher temperatures. It is easily shown that the fraction of molecules containing energy greater than E in one degree of freedom at temperature T is $e^{-E/RT}$; therefore the overall rate of reaction should be

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† A detailed account of the theory is given by Hinshelwood, *The Kinetics of Chemical Change in Gaseous Systems*, Clarendon Press, Oxford, 1945.

$$PZe^{-E/RT},$$

where P is the steric factor, Z the collision frequency. Since Z will vary directly as the concentration of each reactant, we may replace Z by $Z_0[\mathrm{A}][\mathrm{B}]$, where Z_0 is the collision frequency at unit reactant concentration and [A], [B] are the concentrations of reactants. The rate is then given by

$$PZ_0 e^{-E/RT}[\mathrm{A}][\mathrm{B}] = k[\mathrm{A}][\mathrm{B}],$$

so

$$k = PZ_0 e^{-E/RT},$$

where k is the velocity constant.

The rates of most reactions do increase exponentially with temperature, as this expression requires, and from the variation of rate with temperature it is possible to find E, the 'activation energy' of the reaction. (It should be added that Z_0 is not independent of temperature, but its variation with temperature is small compared with that of the exponential term.) When E is known, the 'frequency factor' PZ_0, can be found, and hence P. For a number of reactions P has moderate values (1–10^{-2}) which may well be ascribed to steric effects. In some cases, however, P may be excessively small, even 10^{-8}, while in others P exceeds unity, sometimes by several powers of ten. The simple theory must be modified to explain these abnormal results.

The very small values of P can be explained if the reaction is subject to quantum restrictions. If the reactants can react only if they are in certain limited quantum states, only a small fraction of collisions may lead to reaction, even when the steric and energetic requirements are satisfied. The high values of P can be explained if the activation energy may be shared over several degrees of freedom. If the energy in the rth degree of freedom is E_r, we then require only that

$$\sum_r E_r > E.$$

The fraction of molecules having energy E_r in degree of freedom r is

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† i.e. reactions involving two reactant molecules.

$e^{-E_r/RT}$. The fraction having energy E_1 in the first degree of freedom, E_2 in the second, and so on, is then

$$e^{-E_1/RT}\times e^{-E_2/RT}\times\ldots = e^{-\Sigma E_r/RT}.$$

Therefore the fraction having a total energy $> E$ divided in a specified way between the various degrees of freedom is $e^{-E/RT}$. Hence the fraction having a total energy $> E$ divided at random between the various degrees of freedom is

$$Be^{-E/RT},$$

where B is the number of ways the energy can be partitioned. Therefore the velocity constant will be given by

$$k = PZ_0\,Be^{-E/RT},$$

and since B may be very large, PB, the apparent steric factor, may be much greater than unity.

This general treatment of reaction kinetics is undoubtedly correct in principle, but in practice it suffers from two disadvantages. Firstly, it does not provide any simple method for calculating the frequency factors of reactions *a priori*, and secondly, it gives no very clear picture of the process of activation that leads to reaction. These difficulties have been overcome in an alternative treatment of reaction rates which will be discussed later.

The quantum theory of reactions†

The application of quantum theory to the study of chemical reactions was first attempted by Heitler and London, and their treatment has not yet been improved in any fundamental way. They considered the simplest type of replacement reaction where an atom or radical A replaces an atom or radical C from a neutral molecule B—C, where B and C are singly linked.

$$\mathrm{A\cdot\ B{-}C \rightarrow A{-}B\ \cdot C}$$

The reaction will not much affect either the inner electrons of the three atoms, or the electrons of any substituents attached to them, so to a first approximation we may treat the system as one of three valency electrons moving in the field of three atomic nuclei. Of these electrons, two initially form a pair-bond between B and C, while one is the odd electron on the atom or radical A; in the product two electrons link A and B, while C carries the odd electron.

The simplest way in which reaction could occur would be if the bond B—C were first ruptured, leaving B and C as atoms or radicals and if B then combined with A. In this case reaction could only occur if the reactants had enough energy between them to rupture the B—C bond. The need for activation would then be clear, but in practice the observed activation energies are generally too low for such a mechanism to be possible. The observed activation energies are much less than the energy required to rupture bonds.

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† See pp. 19, 20, for references (Eyring et al.).

Heitler and London found that reaction can occur by an alternative route which requires much less activation. They calculated the energy of the system A—B—C for various separations of the atomic nuclei. First they showed that the energy is least, that is, that the system is most stable, when the nuclei A, B, C are in line; this might be expected from qualitative considerations since the atoms A, C are not directly linked. As we are interested only in the minimum energy that the system must have for reaction to take place, we need only consider linear arrangements of the nuclei. In such a system there are three variables, the distance A—B, the distance B—C, and the total energy. The states of the system could therefore be plotted as a surface in three dimensions, one for each variable; but it is more convenient to represent the surface by a two-dimensional contour map (the contours representing the energy of the system), just as the surface of a mountain is represented by contours more conveniently than by a relief model. When calculations of the energy are carried out for various separations of the nuclei the resulting contour map looks something like Fig. 4.

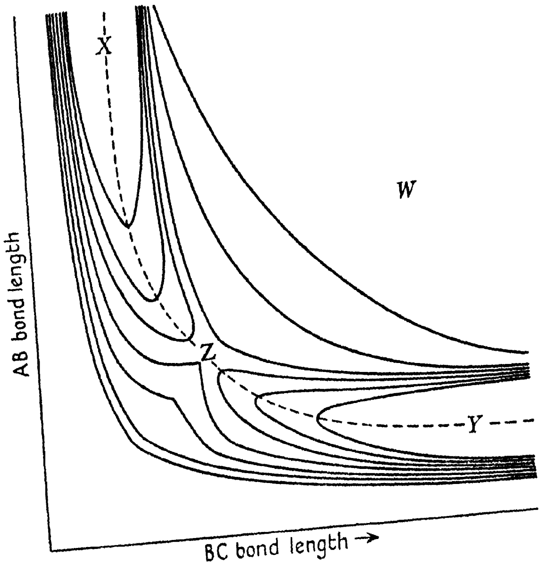


Fig. 4.

The 'valley' *X* represents the initial state of the system, when B, C are at their bonding distance and A is remote, while the 'valley' *Y* represents the final state where A and B have combined and C is far away. In order to cross from *X* to *Y*, that is, in order that reaction may occur, the system must pass through intermediate states of higher energy. Our object is to find a path from *X* to *Y* which will rise as little as possible above the level of the starting-point; the problem is exactly analogous to that confronting a mountaineer who wishes to cross from one valley to another by the easiest route, and our solution, like his, is that the route must cross the 'col' or pass between the valleys at its lowest point *Z*. The easiest path for the reaction is represented in Fig. 4 by a dotted line, and the activation energy will be given by the difference in 'height' between *Z* and *X*. Two points are obvious. Firstly, *Z* is much lower than the 'plateau' *W* which corresponds to a state where A, B, and C are all separated; therefore the activation energy should be less than the energy required to break the BC bond. Secondly, in the state represented by *Z*, A and C are at comparable distances from B, though the distances AB and BC are both greater than the normal bond-lengths. We may deduce that in the intermediate or 'transition state' *Z*, both A and C are bonded to B. The reaction takes place relatively easily because A begins to bond itself to B before the BC bond has broken. If the 'effective' energies of the AB and BC bonds in the transition states are E_2 and E_3, and if the initial BC bond energy is E_1, the activation energy will be not E_1 as the simple theory required, but $E_1 - E_2 - E_3$. For instance, the energy required to break the C—H bond in methane is about 102 Cals., but the activation energy of the reaction

$$H\cdot + H{-}CH_3 \rightarrow H{-}H + \cdot CH_3$$

is only about 13 Cals. In the transition state of this reaction, the total energy of the nascent H—H bond and the weakening C—H bond must be about 90 Cals.

In the transition state, then, all three atoms are held together by the three valency electrons. Moreover, the transition state, being at the top of a potential energy hill, will be in equilibrium, albeit unstable equilibrium. It will in fact be stable to displacements in all directions other than that leading to reaction. Therefore the transition state is a perfectly good molecular species which differs from normal molecules only in that it is unstable to displacements along one 'reaction coordinate'.

Two further points arise. Firstly, the treatment assumes that the system remains throughout in its lowest energy state. This assumption is very reasonable, because electrons are much lighter than atoms and move more rapidly; therefore during reaction the electrons should always have time to adopt their most stable configuration while the nuclei move to and fro. Such reactions where the electron orbitals change continuously are called 'adiabatic', as opposed to 'diabatic' reactions where discontinuous electronic transitions take place (e.g. reversal of electron spins).

Heitler and London considered only atomic replacement reactions, but obviously the same principles must apply to ionic replacements. An anionoid replacement, such as that of iodine in methyl iodide by hydroxyl ion, differs only from an atomic replacement in that four valency electrons are involved, while in a cationoid replacement two electrons only take part. Very few calculations have been made for such systems by the Heitler–London method, but in truth such calculations would be of very little practical value. The approximations necessary for the treatment to be possible are such that the quantitative results are very disappointing. The main value of the method is the clear qualitative picture it gives of the processes underlying chemical reaction.

The transition state theory

The majority of organic reactions can be divided into stages each of which involves a continuous adiabatic reaction of the type Heitler and London considered. In each stage there is a continuous electronic transition from the reactants to the products, and some intermediate or transition state will correspond to the analogous state or energy col in the simple replacement reaction. Such a transition state is a definite molecular species, differing from ordinary molecules only in that it is unstable to displacements along one reaction coordinate; therefore we can attribute to it the normal thermodynamic properties of molecules, heat content, entropy, and so forth. From the principle of microscopic reversibility we may assume that the formation of the transition state from the reactants is reversible. The concentration of the transition state molecules will then be governed by an equilibrium. For a reaction $\mathrm{A}+\mathrm{B}+\mathrm{C}+\ldots+\mathrm{N} \rightarrow \mathrm{A}^* \rightarrow$ products, where A^* is the transition state, we may write

$$\frac{[\mathrm{A}^*]}{[\mathrm{A}][\mathrm{B}]\ldots[\mathrm{N}]} = K^*, \quad \text{or} \quad [\mathrm{A}^*] = K^*[\mathrm{A}][\mathrm{B}]\ldots[\mathrm{N}],$$

where K^* is the equilibrium constant. Now the rate of the conversion of the transition state A^* into the products will be proportional to its concentration, the reaction being effectively unimolecular. Therefore the overall rate of reaction will be

$$k^*[\mathrm{A}^*] = k^*K^*[\mathrm{A}][\mathrm{B}]\ldots[\mathrm{N}].$$

Since the rate will also be given by

$$k_1[\mathrm{A}][\mathrm{B}]\ldots[\mathrm{N}],$$

the rate constant k_1 is given by

$$k_1 = k^*K^*.$$

This result can be expanded in two ways. Firstly, k^* may be calculated by statistical mechanics: it has the same value, kT/h, for all reactions, k and h being the Boltzmann and Planck constants respectively. Secondly, we may use the well-known thermodynamic expression for the equilibrium constant to express K^* in terms of the thermodynamic properties of the transition state: thus

$$RT\log K^* = -\Delta F^* = T\Delta S^* - \Delta H^*,$$

$$K^* = e^{(T\Delta S^*-\Delta H^*)/RT} = e^{\Delta S^*/R}e^{-\Delta H^*/RT},$$

where ΔF^*, ΔH^*, and ΔS^* are the differences in free energy, heat content, and entropy between the initial and transition states; that is to say, they are the free energy, heat, and entropy of activation. We can now write the velocity constant of the reaction as

$$k_1 = k^*K^* = \frac{kT}{h} e^{\Delta S^*/R} e^{-\Delta H^*/RT}.$$

This expression is formally identical with that given by the collision theory if

$$E \equiv \Delta H^*,$$

$$PZ_0 \equiv \frac{kT}{h} e^{\Delta S^*/R}.$$

However, the 'transition state theory' is the more convenient for two reasons. Firstly, it is possible to measure or calculate the entropies of many simple compounds and also to calculate the entropy of the transition state if we care to assume a definite configuration for it. In such cases the entropy of activation, and from it the frequency factor, can be calculated from data quite unconnected with the reaction, and the values so obtained agree excellently with those found experimentally. Secondly, the theory assumes a definite mechanism of activation, and in theory, at least, the activation energy could be calculated by quantum mechanics. Indeed, Eyring and others have developed a semi-empirical extension of the Heitler–London treatment whereby activation energies can be calculated satisfactorily in simple cases from purely spectroscopic data. The transition state theory is therefore able to determine the absolute rates of such reactions fairly accurately without any reference to experiment.

In a 'normal' bimolecular reaction the structures of the reactants are similar in the initial and transition states and the entropy of activation is low. The frequency factor calculated by the transition state theory then agrees with that (Z_0) given by the collision theory with $P = 1$. The high and low values of P correspond to reactions with high or low entropies of activation. If the transition state is made more rigid by such factors as steric hindrance, its entropy will be abnormally low; the entropy of activation will then be low and the frequency factor low also. Conversely, if the reactants are 'loosened' in forming the transition state, the entropy of activation, and so the frequency factor, will be high. Since the entropy of activation appears in the rate expression as an exponential, small changes in it will greatly alter the rate.

CHAPTER III

SOME PROPERTIES OF BONDS

Bond lengths

Several methods are now available for measuring the lengths of bonds in molecules. The general procedures are well known and need not be discussed here, but the results are of immediate importance.

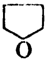
Table 1

Bond-lengths in A

X	C—X	C=X	C≡X	H—X	N—X	N=X
C	1·54	1·33	1·21	1·09	1·47	1·27
N	1·47	1·27	1·15	1·01	1·41	1·24
O	1·43	1·21	. .	0·96	1·37	1·22
F	1·40	. .	. .	. .	. .	. .
Cl	1·77	. .	. .	1·28	1·77	. .
Br	1·91	. .	. .	1·42	. .	. .
I	2·12	. .	. .	1·62	. .	. .
Si	1·93	. .	. .	. .	. .	. .
P	1·87	. .	. .	. .	. .	. .
S	1·82	. .	. .	1·35	. .	. .

Table 2

Observed bond-lengths in A

C—C *bonds*		C=C *bonds*		C—N *bonds*		C—O *bonds*	
Ethane	1·55	$CH_2=CH_2$	1·34	Me_3N	1·47	MeONO	1·44
Neopentane	1·54	$CH_2=C=CH_2$	1·33	Me_2NCl	1·47	Me_2O	1·42
Cyclopentane	1·52	$CH_2=$	1·34	MeN_3	1·47	$(MeO)_3B$	1·43
Diamond	1·54			$MeNO_2$	1·47		1·43
Glycine	1·52			MeN=NMe	1·47		
Chloral	1·52			$C(NO_2)_4$	1·47		

The length of a given bond is found to be almost identical in different compounds, provided that the bond is not incorporated into a conjugated system. Average values for the lengths of a number of bonds are given in Table 1, and Table 2 illustrates how little the lengths vary from one compound to another. This result might have been anticipated, because an unconjugated bond is little affected electronically by neighbouring bonds, and so its main properties should be more or less independent of its environment. The length is obviously one such property. (Incidentally, the experimental errors in the values given in Table 2 are mostly 0·02–0·03 A.)

A conjugated π-bond has, however, a fractional order, and we might therefore expect its length to be intermediate between the lengths of 'pure' single, double, and triple bonds. The following examples show that such is the case:

Butadiene (central bond)	1·46	C—C	1·54
Benzene	1·39	C=C	1·33
Cyanogen	1·37	C≡C	1·20
Diacetylene (central bond)	1·36		

We might indeed expect a quantitative relation to hold between the length and order of a bond. Pauling and others have shown theoretically that such a relation should exist. An empirical curve connecting the two for C—C bonds was reproduced earlier (p. 12). From the curve and the measured length of a bond it is possible to determine its order, and the bond orders so found for a number of hydrocarbons agree very well with the values calculated by quantum mechanics. Evidently measurement of bond-length is a most valuable method for finding out whether bonds are conjugated. An interesting application of this principle has been found in various methylacetylenes where the CH_3—C bonds are much shorter than normal single C—C bonds and obviously have an order greater than 1. This would be expected if methyls can hyperconjugate with multiple bonds, and the effect is one of the most convincing proofs that hyperconjugation does in fact occur in such compounds.

Me—C *bond-lengths*

Me—C≡CH	1·46	(C—C 1·54)
Me—C≡C—Me	1·47	
Me—C≡C—C_2H_3	1·47	
Me—C≡C—C≡C—Me	1·47	

It is also interesting that the C—C bonds in the rings of benzene and hexamethylbenzene are all of exactly the same length, as of course must be the case if the quantum-mechanical treatment of benzene is correct. The complete symmetry of benzene has also been established by spectroscopic measurements.†

Bond-energies

Another fundamental property of a molecule is its heat of formation from atoms. This heat of formation (ΔH) may be written as

$$\Delta H = \Delta E_0 - H_M + H_A,$$

where ΔE_0 is the potential energy of formation (that is, the difference between the total energy of the electrons in the molecule and in the atoms from which it is formed), H_M is the kinetic energy of the molecule, and H_A the total kinetic energy of the atoms. Heats of formation of organic compounds are generally deduced by well-known thermochemical methods from their heats of combustion. The heat of combustion of a compound M, that is, of the reaction

$$M + xO_2 \rightarrow yCO_2 + zH_2O + \text{etc.}$$

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† Ingold et al., *J.C.S.* 1936, 912 et seq.; 1946, 222 et seq.

is equal to the difference between the heats of formation of ($M+xO_2$) and (yCO_2+ etc.). Since the heats of formation of O_2 and the products of combustion are known, the heat of formation of the compound can so be found. An example will be given later.

Since in an unconjugated molecule the various bonds are usually little affected by the rest of the molecule, we might expect the energy of the electrons forming such a bond to depend only on the terminal atoms. In that case the potential energy of formation (ΔE_0) of the molecule should be expressible in terms of the potential energies of formation (δE_0) of the bonds, the δE_0 of a given bond being the same in different compounds. Unfortunately it is difficult to estimate ΔE_0, but Pauling showed some time ago that a similar relation held for ΔH, the heats of formation of unconjugated compounds being an additive function of the heats of formation of individual bonds (bond-energies). He gave a table of bond-energies which has been generally accepted and widely used for calculating heats of formation.

TABLE 3

Bond-energies and heats of formation in Cals./Mol.

	H	C	N	O	S	F	Cl	Br	I
H	103·4	98·6	101·7	117·2	94·5	147·5	102·7	87·3	71·4
C—	..	81·1	77·9	88·2	72·8	118·3	77·8	65·3	56·8
C=	..	145	152·5	178·5† 185·5‡ 188·5§	140	..	..	..	..
C≡	..	190·5	238	..	..	..	..	..	..
O—	..	..	87·5	66	..	65·6	56·3	..	..
O=	..	..	161	..	..			..	..
N—	..	..	60			86·8	56·4		
N=	..	..	152						

O_2	146·2	HF	147·5
CO_2	410·7	HCl	102·7
H_2O (liquid)	244·9	Br_2 (vapour)	46·2
N_2	278·2	I_2 (solid)	51·2
SO_2	297·4		

† Refers to CH_2O; ‡ refers to $R{\cdot}CHO$; § refers to ketones.

The values have mostly been recalculated from those given by Pauling (*The Nature of the Chemical Bond*, Cornell, 1945) and refer to heats of formation of the vapour at 25°.

In recent years it has become increasingly evident, however, that the absolute values of many of the bond-energies given by Pauling are unsatisfactory from the chemist's point of view. The chemist is primarily interested in bond-strengths rather than bond-energies, that is, in the energy required to break one bond in a molecule while the rest of the molecule remains intact. Thus Pauling's value for the C—C bond-energy is 58·6 Cals., but about 80 Cals. are required to break the C—C bond in ethane to form two methyl radicals. It is, however, possible to modify the bond-energy table so that the values for the bond-energy and bond-strength of any bond are equal if we take the heat of formation to refer to formation from atoms in arbitrary energy states. Since the modified bond-energies are equally useful in all thermochemical calculations, it seems more sensible to give them rather than separate tables of bond-energies and bond-strengths. This has been done in Table 3, where modified heats of formation of oxygen and CO_2, H_2O, etc., are also given. The problem is discussed more fully in a note at the end of the chapter.

We may illustrate the use of this table by calculating the heat of formation of ethylamine from the heat of combustion of its vapour at 25°, 413 Cals. We have

$$C_2H_5NH_2+3\tfrac{3}{4}O_2 = 2CO_2+3\tfrac{1}{2}H_2O+\tfrac{1}{2}N_2+413 \text{ Cals.}$$

The heat of formation of $3\frac{3}{4}O_2$ is 548 Cals. That of the oxidation products is $(2\times 410{\cdot}7)+(3\frac{1}{2}\times 244{\cdot}9)+(\frac{1}{2}\times 278{\cdot}2) = 1817{\cdot}6$ Cals. Therefore the heat of formation of ethylamine is $1817{\cdot}6-413-548{\cdot}3 = 856{\cdot}3$ Cals. The heat of formation calculated from Table 3 is

$$5E_{\mathrm{CH}}+E_{\mathrm{CC}}+E_{\mathrm{CN}}+2E_{\mathrm{NH}} = 493+81{\cdot}1+77{\cdot}9+203{\cdot}4 = 855{\cdot}4 \text{ Cals.}$$

The accuracy with which the heats of formation of unconjugated compounds can be predicted is shown by the following typical examples.

TABLE 4

	ΔH *obs.* (*Cals.*)	ΔH *calc.* (*Cals.*)
Methane	414	412
Ethane	690	690
Propane	968	968
Propylene	834	835
1-Butene	1,112	1,113
Acetylene	389	386
Ethanol	681	680
n-Butanol	1,240	1,237
Dimethyl ether	797	795
Diethyl ether	1,356	1,353
Acetaldehyde	570	571
Methylamine	590	591
Ethylamine	870	870
Methyl chloride	389	388
Ethyl bromide	583	582
Acetonitrile	635	629

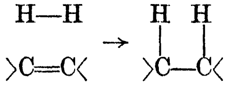
A conjugated compound is, however, more stable than a single classical bond-structure for it would suggest. Therefore the observed heat of formation of a conjugated compound is greater than that of an unconjugated isomer, and thus greater than the value calculated from the bond-energy table. This difference in heat of formation is a measure of the stabilization due to conjugation, and Pauling has called it the 'resonance energy'. Some examples are given in the following table.

TABLE 5

Resonance energy (Cals.)

Benzene	41	Acetic anhydride	41
Toluene	41	Methyl propionate	21
Naphthalene	77	Acetamide	25
Anthracene	116	Furane	24
Phenanthrene	130	Thiophene	29
Pyrene	152	Pyrrole	24
Chrysene	163	Indole	63
Biphenyl	91	Pyridine	40
Fluorene	101	Quinoline	75
Phenol	50	Azulene†	46
Aniline	51	Cyclo-octatetraene‡	12
Formic acid	18		

Unfortunately resonance energies cannot easily be found from heats of combustion of organic compounds since the heats of combustion are so large and the resonance energies relatively small. Even in the case of benzene the resonance energy is only 4 per cent. of the total heat of combustion and a small error in measuring the latter will greatly affect the resonance energy calculated from it. In the case of polyenes and other compounds with low resonance energies the resonance energy becomes comparable with the experimental error in measuring the heat of combustion. Kistiakowsky and his collaborators§ have therefore introduced an alternative method of measuring resonance energies of unsaturated hydrocarbon derivatives from their heats of hydrogenation. The heat of hydrogenation of an olefine is the heat of the reaction:



$$\begin{matrix} H{-}H \\ \rangle C{=}C\langle \end{matrix} \rightarrow \begin{matrix} H \quad H \\ | \quad\; | \\ \rangle C{-}C\langle \end{matrix}$$

In the reaction an H—H bond and a C—C π-bond are broken and two C—H bonds are formed. The heat of reaction (ΔH) should therefore be

$$\Delta H = 2E_{CH} - E_{C=C} - E_{HH},$$

where E_{CH}, E_{HH} are the bond-energies of the CH and HH bonds, $E_{C=C}$ of the C—C π-bond (i.e. the difference between the heats of formation of C=C and C—C). The heat of hydrogenation should therefore be constant in unconjugated olefines. A conjugated olefine will, however, be more stable by an amount equal to its resonance energy, E_R. This resonance energy will be lost in the reduction, so the heat of hydrogenation will be

$$\Delta H = 2E_{CH} - E_{C=C} - E_{H-H} - E_R$$

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† Heilbronner and Wieland, *Helv. Chim. Acta*, 1947, **30**, 953.

‡ Prosen, Johnson, and Rossini, *J.A.C.S.* 1947, **69**, 2068.

§ *J.A.C.S.* 1935, **57**, 65, 876; 1936, **58**, 137, 146; 1937, **59**, 831; 1938, **60**, 440, 2764; 1939, **61**, 1868; *Chem. Rev.* 1937, **20**, 181.

and will be less than that of an unconjugated analogue by E_R, that is, by the resonance energy. Heats of hydrogenation are relatively small, so resonance energies can be found much more accurately from them than from heats of combustion. Some values for heats of hydrogenation found by Kistiakowsky are given in the following table. They show clearly, not only the effects of conjugation in conjugated polyenes, but also the effect of hyperconjugation in simple olefines. Thus in propylene the methyl is hyperconjugated with the double bond and its heat of hydrogenation is therefore less than that of ethylene. This effect increases, as it should, with the number of alkyl substituents attached to the double bond. The resonance energies of the conjugated polyenes are calculated by comparing their heats of hydrogenation with unconjugated analogues. This eliminates the extra effects due to hyperconjugation.

TABLE 6

Ethylene	32·8		2-Butene (*cis*)	28·6	mean 28·2
Propylene	30·1	mean 30·2	2-Butene (*trans*)	27·6	
1-Butene	30·3		2-Pentene	28·0	
1-Heptene	30·1		Cyclohexene	28·6	
tert-Butylethylene	30·3		*iso*-Butene	28·4	
			Trimethylethylene	26·9	
			Tetramethylethylene	26·6	

		ΔH *obs.*	ΔH *calc.*	E_R
Unconjugated	1:4-Pentadiene	60·8	60·4	—
	1:5-Hexadiene	60·5	60·4	—
	Limonene	54·1	55·1	—
Conjugated	1:3-Butadiene	57·1	60·4	3·1
	1:3-Pentadiene	54·1	58·4	4·3
	α-Terpinene	50·7	53·8	3·1
	1:3-Cyclohexadiene	55·4	56·4	1·0
Aromatic	Benzene	49·8	84·6	34·8
	Styrene	77·5	113·6	36·1
	Indene	69·9	111·6	41·7

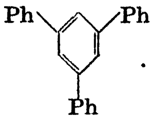
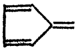
We have so far accepted without question Pauling's idea that heats of formation are actually additive functions of bond-energies. Now in the expression (p. 31)

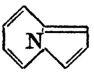
$$\Delta H = \Delta E_0 - H_M + H_A$$

additivity in ΔH implies additivity in the other terms. In an unconjugated compound it is reasonable to assume that the potential energy of formation will be the sum of the potential energies of formation of individual bonds, the latter 'binding energies' as we may call them, following Wheland, being the same in different compounds. The kinetic energy H_M of the molecule will, however, depend on its modes of vibration and rotation as a whole, and so we would not expect H_M to be an additive function of the bonds in it. The additivity of bond-energies is therefore an unexpected result and we must be ready to find exceptions to it. Indeed it has recently been shown† that serious deviations do occur in compounds whose molecules are for some reason unusually rigid. In such compounds the total kinetic energy seems to be abnormally low and hence the observed heat of formation is higher than that calculated. Thus the calculated heats of formation of a number of acetals are considerably lower (*c.* 15 Cals.) than the observed values; yet these compounds are not mesomeric and the 'resonance energies' calculated by Pauling and Sherman's method must be quite spurious. These acetals must be abnormally rigid since mutual repulsion of the C—O dipoles will restrict the free rotation of the alkoxyl groups. The same effect probably accounts for a large part of the observed 'resonance energies' of carboxylic acid derivatives which are much larger than theoretical considerations would suggest.

The effect seems to be important in cyclic compounds, which are naturally more rigid than their open-chain counterparts, and to become large in polycyclic structures. In such compounds the Pauling–Sherman method of calculating resonance energies from heats of combustion seems to be quite erroneous. The Kistiakowsky method is more satisfactory since the spurious resonance energies of the aromatic compound and its reduction product should be comparable, and Kistiakowsky effectively measures the difference in resonance energy between the two structures. Unfortunately the heats of hydrogenation of aromatic compounds have been little studied, but Dewar has shown that the thermal data support the values for resonance energies found by quantum-mechanical calculation. Some values so calculated‡ are given in Table 7.

TABLE 7

Substance	*Resonance energy Cals./mol.*
Benzene	36
Diphenyl	75
Naphthalene	62
Anthracene	87
Phenanthrene	92
Pyrene	107
Styrene	40
Stilbene	79
$Ph_2C{=}CH_2$	81
	154
	21

Substance	*Resonance energy Cals./mol.*
Azulene	53
Vinylamine	5
Aniline	40
Pyrrole	25
Indole	56
iso-Indole	56
	52
Pyridine	31
Pyrimidine	26
Piperazine	27
1, 3, 5-Triazine	20
Iminazole	27
Quinoline	56

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† Dewar, *Trans. Faraday Soc.* 1946, **42**, 767.

‡ The values for hydrocarbons were calculated by Wheland, *J.A.C.S.* 1941, **63**, 2025, by an improved molecular orbital method. The values for nitrogen compounds were calculated by a more approximate method by the author (see Dewar, *Trans. Faraday Soc.* 1946, **42**, 764).

Polarity and polarizability

In some molecules the centres of negative charge on the electrons and of positive charge on the nuclei coincide. Such molecules will show little tendency to orient themselves in an electric field and are called non-polar. For instance, a homonuclear diatomic molecule like Cl_2 will be non-polar since it is completely symmetrical. In other molecules the centres of charge do not coincide; thus in hydrogen chloride the chlorine gets a lion's share of the bonding electrons and the centre of negative charge is displaced towards chlorine. In an electric field such a 'polar' molecule will try to orient itself parallel to the field. Hydrogen chloride, for instance, will try to orient itself with the negative chlorine towards the positive side of the field and with the positive hydrogen towards the negative side. In a polyatomic molecule two or more bonds may be polar; the polarity of the whole molecule will then be the vector sum of the individual moments (which are vector, not scalar, quantities). It is possible for a molecule to be non-polar as a whole even though it contains polar bonds. Carbon tetrachloride is non-polar, although the individual C—Cl bonds in it are certainly highly polar, because in it the four C—Cl electric vectors cancel.

It is not possible to measure the individual bond-moments in a molecule but only its total polarity, which is the vector sum of the individual bond-moments. If, however, we assume that the moment of an unconjugated bond is another property independent of its environment, and if we make certain basic assumptions about the moment of the C—H bond, it is possible to calculate values for the moments of individual bonds, such that the total electric dipole moment of a molecule is the vector sum of the individual bond-moments. These moments are of the order of 10^{-18} e.s.u., since bond-lengths are of the order of 1 A (= 10^{-8} cm.), and the electronic charge is of the order of 10^{-10} e.s.u. They are therefore usually measured in Debye units (D) where 1 D = 10^{-18} e.s.u. Such moments for a number of common bonds are given in Table 8.

TABLE 8

+ −		+ −	
C—H	0·4	H—I	0·38
H—N	1·31	C—N	1·25
H—O	1·51	C—O	1·6
H—S	0·68	C—Cl	2·3
H—Cl	1·03	C—Br	2·2
H—Br	0·78	C—I	2·0

The negative end of the vector is usually directed towards the atom with the larger atomic number, as one would expect, since, having the greater nuclear charge, it will attract the bond electrons more strongly. The dipole moments of most unconjugated compounds can be represented quite accurately as the vector sum of their bond-moments. A polar bond is generally represented in formulae by an arrow pointing towards the negative end of the dipole, or by writing partial charges on the atoms; thus: H→Cl, or $\overset{\delta+}{\mathrm{H}}\text{—}\overset{\delta-}{\mathrm{Cl}}$.

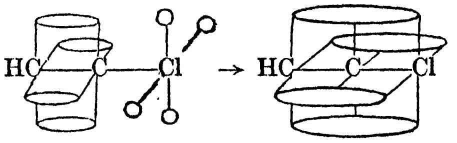
The origin of bond polarity was discussed in Chapter I; it is the uneven sharing of the bonding electrons between the bonded atoms. It was also pointed out there that a continuous transition should be possible between 'pure' electrovalent bonds where both electrons are completely localized on one of the atoms, and 'pure' symmetrical covalent bonds. It is interesting that the moments of many salts, e.g. KCl, are smaller than would be expected if electron transfer were complete, indicating that the bonds in them may not be purely electrovalent; the positively charged potassium ion deforms the electron atmosphere of the chlorine union by electrostatic attraction, so that the electron orbitals approximate somewhat to normal covalent bond orbitals.

Conjugation alters the electron distribution in a molecule and so affects its dipole moment. Thus in vinyl chloride the chlorine conjugates with the double bond. Two of the p-electrons of chlorine and the two π-electrons forming the double bond then occupy extended orbitals covering all three atoms. Since the chlorine contributes more than its fair share of these four electrons, the effect of conjugation is to deprive the chlorine of part of its electronic atmosphere. The chlorine therefore acquires a positive charge and the carbon atoms a negative one; the conjugation therefore produces an electric moment in the compound.

$$\overbrace{\mathrm{CH_2 \mathrel{\dot{=}} CH}}^{\delta-} \mathrel{\dot{=}} \overset{\delta+}{\mathrm{Cl}}$$

Now this moment is opposite in direction to the normal $\mathrm{C \rightarrow Cl}$ bond moment; therefore conjugation reduces the total dipole moment in vinyl chloride. The effect is clearly seen from the values for total moments given in Table 9.

The vinyl halides are less polar than the corresponding ethyl halides. In ethinyl halides the effect is still greater. The halogen has two pairs of p-electrons which can conjugate with both π-orbitals of the $\mathrm{C \equiv C}$ triple bond, as indicated in the following diagram:



or $\overbrace{\mathrm{HC \mathrel{\dot{\equiv}} C}}^{\delta-} \mathrel{\dot{\equiv}} \overset{\delta+}{\mathrm{Cl}}$

The charge transfers are therefore still greater than in the corresponding vinyl halides (Table 9), and bromoacetylene is actually non-polar.

A similar effect is observed in phenyl halides, and for the same reason.

The measurement of dipole moments is therefore of value for two reasons. Firstly, the moment of a molecule gives an indication of the distribution of the valency electrons in it, and in particular provides a sensitive test for conjugation. Secondly, since bond-moments add vectorially, the total moment of an unconjugated compound gives some information about its stereochemistry.

TABLE 9

X	Dipole moment of			
	CH_3—CH_2—X	CH_2═CH—X	CH≡C—X	Ph—X
Cl	2·05	1·44	0·44	1·73
Br	2·02	1·41	0·0	1·71
I	1·90	1·26	..	1·50

Data from Wiswall and Smyth, *J. Chem. Phys.* 1941, **9**, 356; Hugill, Coop, and Sutton, *Trans. Faraday Soc.* 1938, **34**, 1518.

Diamagnetic susceptibility

Electrons have the property of ' spin ', that is, according to the classical representation they are clouds of negative electricity in rotation. Now in classical theory such rotation of a charge is equivalent to the flow of a current in a circle and so an electron should possess a magnetic field and function like a miniature magnet. Such is indeed the case. Moreover, the motion of a valency electron in its orbital is again equivalent to the flow of a current in the locus of its motion, and so an electron should also possess a magnetic moment in virtue of its orbital motion; but the moment due to orbital motion is generally less important than the spin moment. These conclusions are confirmed by the deflexion of a beam of hydrogen atoms on passage through an inhomogeneous magnetic field, the atoms being deflected according to their orientation with respect to the field (Stern–Gerlach experiment).

In a 'normal' molecule, where all the valency shells of the atoms are filled, the electrons occupy the various orbitals in pairs with opposite spin. Thus the magnetic moment of each electron is neutralized by an equal and opposite moment due to its partner, and since, moreover, the orbital magnetic moments of the electrons in a full valency shell cancel, such molecules have as a whole no permanent magnetic moment.

Now it is easily shown that a molecule without a permanent magnetic moment will be *diamagnetic*, that is, if placed in an inhomogeneous magnetic field it will move in the direction of diminishing field strength. By measuring the total force exerted by a known field on a known weight of a substance we can obtain a quantitative measure of its *diamagnetic susceptibility*. The quantity of most interest is the molar susceptibility, the force exerted on one mole of a substance by a field of unit gradient.

Bond susceptibilities

Pascal found that the molar diamagnetic susceptibilities of a number of compounds were additive functions of the atoms in them, together with special contributions for various structural features (e.g. double bonds). Following the modern practice his results have been recalculated to give additive bond-susceptibilities.

Bond-susceptibilities (*in* 10^{-6} *e.s.u.*)

C—H	−4·43	N—H	−4·79
C—C	−3·00	O—H	−5·23
C—N	−3·36	S—H	−10·4
C—O	−3·80	C=C	−0·5
C—F	−13·0	C≡C	−8·2
C—Cl	−21·6	C=O	−1·27
C—Br	−32·1	C=N	+1·5
C—I	−46·1	N=N	−5·64
C—S	−9·0		

Structural corrections (*in* 10^{-6} *e.s.u.*)

Ester, carboxyl	+1·25	C=C—C=C	−0·4
Amide	+4·03	Benzene	−1·44
Imide	+3·46	Naphthalene	−8·12
Cyclohexane	+3·0		

The structural corrections arise mainly in mesomeric compounds, though in truth it is now evident that the additivity of magnetic susceptibility is only approximate even in non-conjugated systems. However, the values given above are often useful for calculating approximate susceptibilities of compounds (see, for example, the next section).

Paramagnetic susceptibility

A radical, on the other hand, contains at least one unpaired electron, whose spin magnetic moment will be uncompensated. Such a molecule should have a permanent magnetic moment and function like a magnet. In an inhomogeneous magnetic field it will be attracted in the direction of increasing field strength, and the *molar paramagnetic susceptibility* of such a substance is defined as the force exerted on one mole of it by a field of unit gradient.

Of course the observed susceptibility of a radical will be the difference between the paramagnetic susceptibility due to the odd electron and the diamagnetic susceptibility due to the remaining (paired) electrons. The two contributions cannot be measured independently, but the latter can be estimated with sufficient accuracy from the bond-susceptibility table; for the paramagnetism due to the odd electron is of a different order of magnitude to the diamagnetism due to paired electrons, and so the correction for the latter is relatively small.

The application of magnetic measurements to the study of stable free radicals will be discussed later (Chapter XII).

Other additive properties of bonds

Organic chemists have spent much effort in attempts to find properties of molecules which should be additive functions of their component atoms and structure, their object being to use such properties as aids in determining structure of compounds. This aim is no longer of much importance since far more information can usually be gained from modern physical methods of investigation (X-ray crystallography, electron diffraction, etc.). However, a number of properties were found to be generally additive and this additivity is of some interest to us in that it usually broke down only in the case of compounds which we should now class as mesomeric. Evidently the properties in question are essentially properties of bond electrons and are additive functions of bonds only so long as the latter are not disturbed by conjugation. This, for instance, is obviously true of molecular refraction, the molecular refraction being a measure of the total polarizability of a molecule; the polarizability of an unconjugated molecule is roughly equal to the sum of the polarizabilities of the individual bonds, but the polarizability of the extended π-orbitals in conjugated systems is abnormally high and so conjugated compounds usually show an 'exaltation' of molecular refraction.

Exactly similar remarks apply to other additive properties such as magneto-optic rotation.

ADDENDUM: THE BOND-ENERGY TABLE

The normal definition of bond-energies is that the total energy required to dissociate a compound into atoms should be equal to the sum of the bond-energies of the bonds in it. Thus the C—H bond-energy is taken to be one-quarter of the heat of dissociation of methane into atoms. Now there is no reason to suppose that the energies required to remove successive hydrogen atoms from methane are equal. The methyl radical, for example, has a different electronic structure from methane and the energy required to remove a hydrogen from it need not be equal to that required to form methyl from methane. In organic chemistry, however, we only wish to know the energy required to break one bond in a compound. Reactions in which two bonds break simultaneously are rare. Therefore to be useful our table of bond-energies should rather give the energies required to break single bonds in a molecule.

It has been usual in the past to determine bond-energies from the heats of formation of compounds from atoms in their ground state. It is equally possible to use other states of atoms as standards. The absolute values of the bond-energies so obtained will be different, but they will be entirely self-consistent. Of course the heats of formation of products of combustion must also be calculated for the same states of their component atoms that are used in calculating bond-energies.

There has been much discussion in recent years about the heat of atomization of carbon, a quantity which of course enters all our calculations. Two values have been favoured, 125 Cals. (the one used by Pauling) and 170 Cals.

From these values two different sets of bond-energies can be derived. From our point of view the controversy is purely academic. The heat of atomization of carbon depends on the energy-state of carbon atoms which we choose as the standard. For our purpose, this energy-state should be regarded as an arbitrary parameter, the value of which should be so chosen that the bond-energies of carbon bonds should be equal to their breaking energy. We should not necessarily accept any of the values corresponding to known energy-states of atoms, although actually the value 170 Cals. for the heat of atomization of carbon leads to a C—C bond-energy close to its observed† breaking energy.

Similar considerations apply to other atoms. Thus the bond-energies O—O, N—N, given by Pauling (35, 20 Cals. respectively) must be much too low, since otherwise compounds containing such bonds would be very unstable. (Hydrazobenzene would be expected to decompose completely in a small fraction of a second at room temperature, if the N—N bond-energy were only 20 Cals.) The observed O—O bond-breaking energy in linoleic acid peroxide‡ is 65 Cals. Although there is some evidence that the O—O bond-energy varies in different compounds, the latter value is much larger than any found from thermochemical data. In Table 3 the reference states of O and N have been so chosen that the bond-energies of bonds containing them correspond to reasonable values for their breaking energies. No direct estimates for nitrogen are available, but a rough value can be found from the rate§ of decomposition of hydrazobenzene in alcohol at 140°, assuming a normal frequency factor and assuming that in the fission to phenylimine radicals the mesomerism of the latter weakens the N—N bond to the same extent as that of the phenyls in dibenzyl weakens the central C—C bond (cf. Chapter XII).

These conclusions are further supported by a recent determination of the OH bond-strength in water.‖ The energy required to convert water into H+OH is 118 Cals., while the heat of formation of water from normal atoms is only 220 Cals.—i.e. the bond-energy O—H as normally defined is 110 Cals.

No evidence is available for the strengths of sulphur bonds, but it seems likely that they are again greater than Pauling's values for the bond-energies. In constructing Table 3 it has been assumed that the difference is the same as in oxygen (7 Cals. per S-link). In confirmation, it may be observed that the ability of R—S-radicals to dehydrogenate hydrocarbons indicates strongly that the S—H and C—H bonds have similar strengths.

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† For a survey of the data on bond-breaking energies see Steacie, *Atomic and Free Radical Reactions*, Reinhold, 1946.

‡ Bolland and Gee, *Trans. Faraday Soc.* 1946, **42**, 244.

§ Stieglitz and Curme, *Ber.* 1913, **46**, 911.

‖ Dwyer and Oldenberg, *J. Chem. Phys.* 1944, **12**, 351.

CHAPTER IV

GENERAL PRINCIPLES OF THE ELECTRONIC THEORY

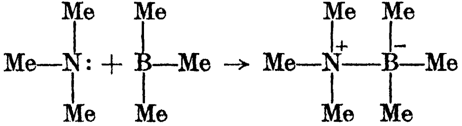
Generalized ionic reactions

ORGANIC reactions can be divided into two main types. In the first, all the reactants and products are composed of 'normal' molecules, each containing an even number of electrons in pairs with opposite spin. In the second, at least one reactant and/or one product is a radical—i.e. a compound whose molecules contain 'odd' unpaired electrons.

If the number of electrons ($2n$) in a molecule is even, the molecule will as a rule be 'normal'; for the energy-levels of the various atomic and molecular orbitals in it will generally differ, and the $2n$ electrons will therefore occupy in pairs the n orbitals of lowest energy. According to the Pauli principle, the electrons of each pair will have opposite spins. Exceptions to this rule occur only in certain molecules with incomplete electron shells, where the highest occupied level is degenerate (i.e. is one member of a group of levels of identical energy). It may then be possible for the outermost pair of electrons to occupy separate orbitals both of the same energy; and if so the lowest energy state will be a 'triplet' state where the electrons have parallel spins, so that the molecule contains two 'odd' electrons and is thus a diradical. The oxygen molecule is the only common example of such a diradical (cf. p. 18), and so for the present we may ignore the rare cases where even-electron organic molecules possess radical character.

In the intermediate (transition) state of a reaction between normal molecules, the same principles will apply. The transition state is a normal molecular species (p. 28), and in a reaction of this type it will contain an even number of electrons. The electrons will occupy in spin-coupled pairs the set of lowest energy orbitals available. Therefore in these reactions electrons are transferred in pairs from one atom or bond to another.

Now if a bond is formed by transfer of a pair of electrons, both bond electrons must be provided by one of the atoms concerned. In the product each of the two bonded atoms has a half-share in two electrons, i.e. the equivalent of one electron. In the original unbonded atoms, one atom had both electrons and the other none. Thus the formation of a bond by electron-pair transfer involves a transfer of negative charge. If the reacting atoms are neutral, the product will contain a polar dative bond (p. 6); a simple example is the union of trimethylamine and trimethylboron to form the compound (I).



$$\mathrm{Me{-}\underset{Me}{\overset{Me}{N}}{:} + \underset{Me}{\overset{Me}{B}}{-}Me \rightarrow Me{-}\underset{Me}{\overset{Me}{\overset{+}{N}}}{-}\underset{Me}{\overset{Me}{\overset{-}{B}}}{-}Me} \qquad (1)$$

(I)

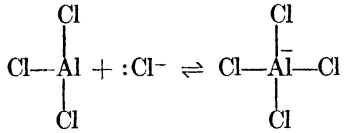
Conversely, in the 'normal' fission of a bond one of the bonded atoms acquires both bond electrons, and clearly there will again be a charge transfer. If the original compound was neutral, the fission products will be ions. A simple example is the ionization of a weak acid (ignoring for simplicity the solvation of the resulting proton).

$$\mathrm{H{:}A} \rightarrow \mathrm{H^+} + \mathrm{{:}A^-} \qquad (2)$$

Naturally the charge distribution in the products of such reactions depends on the charge distribution in the reactants. Thus the bond-fission involved in the reverse of reaction (1), the dissociation of the complex (I) into its components,

$$\mathrm{Me_3\overset{+}{N}{-}\overset{-}{B}Me_3} \rightarrow \mathrm{Me_3N{:}} + \mathrm{BMe_3} \qquad (3)$$

is precisely analogous to the ionic dissociation reaction (2); but in (3) the products are neutral molecules, in (2) ions. Two other possibilities are illustrated in equations (4) and (5).



$$\begin{array}{c}\mathrm{Cl}\\ |\\ \mathrm{Cl{-}Al}\\ |\\ \mathrm{Cl}\end{array} + \mathrm{{:}Cl^-} \rightleftharpoons \begin{array}{c}\mathrm{Cl}\\ |\\ \mathrm{Cl{-}\overset{-}{Al}{-}Cl}\\ |\\ \mathrm{Cl}\end{array} \qquad (4)$$

$$\mathrm{H^+} + \mathrm{{:}NMe_3} \rightleftharpoons \mathrm{H{-}\overset{+}{N}Me_3} \qquad (5)$$

It is therefore evident that 'normal' reactions are essentially analogous to ionic dissociations and recombinations; and we may therefore call them 'generalized ionic reactions', or simply 'ionic reactions' when our meaning is unambiguous.

Although the dissociation and recombination reactions are the basic units, a third type of ionic process may be distinguished. In a reaction an atom may form one bond by donating an electron pair, while breaking another bond by appropriating the bond electrons. The total number of bonds and electrons on the atom thus remains unchanged, and so its charge is not altered. The simplest case is the Heitler–London replacement reaction (p. 25), where the reagent is an anion instead of a radical; thus in the alkaline hydrolysis of methyl iodide,

$$\mathrm{H\overset{-}{O}} + \mathrm{Me{-}I} \rightarrow \mathrm{\overset{\delta-}{H}O...Me...\overset{\delta-}{I}} \rightarrow \mathrm{HO{-}Me} + \mathrm{\overset{-}{I}},$$

the methyl remains approximately neutral, the positive charge produced in it by ionization of the C—I bond being neutralized by donation of electrons by the hydroxyl anion.

Types of reagent

Reactants in ionic reactions may therefore be divided into three categories; reactants whose negative charge decreases, reactants whose negative charge increases, and reactants which remain neutral. Those of the first category correspond to the anion in a simple recombination reaction, e.g. to Y^- in the reaction

$$X^+ + Y^- \rightarrow X\text{—}Y.$$

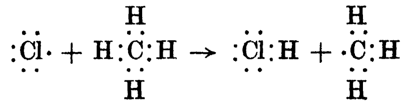
Similarly those of the second category correspond to the cation. Lapworth therefore termed reagents of the first type generalized anions or *anionoid reagents*, those of the second type generalized cations or *cationoid reagents*.[†] The terms refer to the change of charge during reaction, not to its sign. The terms anionoid and cationoid can also be applied to any group or substituent whose net charge changes during a reaction, and by a further generalization to groups or compounds which tend to act as electron donors (anionoid) or electron acceptors (cationoid).

A generalized ionic reaction may thus be pictured as a kind of miniature electrolysis in which chemical change is brought about by flow of electrons from an anionoid group or molecule to a cationoid one, possibly through an intermediate conducting system of atoms which remains neutral.

Radical reactions

When a single bond is formed by the union of two atoms or radicals, no displacement of charge occurs. The bond is formed by sharing of two electrons and each atom or radical contributes one of them. Likewise the rupture of a bond to form two neutral atoms or radicals involves no displacement of charge. Ingold has suggested the term *homopolar* to describe bond-formation and bond-fission where each atom or radical contributes or acquires one of the bond electrons; in contrast to ionic or *heteropolar* reactions where the bond is formed or broken unsymmetrically.

The majority of radical reactions involve only the homopolar fission and formation of bonds and such reactions therefore do not involve displacement of electric charge. However, any reaction of a radical with a 'normal' molecule must *ipso facto* give rise to a new radical since the reacting system contains an odd number of electrons. [A simple example is the Heitler–London replacement:



$$:\underset{\cdot\cdot}{\overset{\cdot\cdot}{\mathrm{Cl}}}\cdot + \mathrm{H}:\underset{\underset{\mathrm{H}}{\cdot\cdot}}{\overset{\overset{\mathrm{H}}{\cdot\cdot}}{\mathrm{C}}}:\mathrm{H} \rightarrow :\underset{\cdot\cdot}{\overset{\cdot\cdot}{\mathrm{Cl}}}:\mathrm{H} + \cdot\underset{\underset{\mathrm{H}}{\cdot\cdot}}{\overset{\overset{\mathrm{H}}{\cdot\cdot}}{\mathrm{C}}}:\mathrm{H}$$

Initially the chlorine atom has an unpaired electron, while all the electrons attached to carbon are paired. In the products the chlorine is saturated while the carbon carries the odd electron.] The main theme in radical reactions is the transfer through the reacting system of the unpaired electrons, just as in ionic reactions the main theme is a displacement of electron-pairs and hence of net electric charge.

[†] Later Ingold suggested the alternative terms nucleophilic for anionoid, electrophilic for cationoid, but there seems to be little reason for adopting them in preference to the earlier nomenclature.

General principles of the electronic theory of reactions

Any reaction which is stoichiometrically possible must be capable of occurrence. If such a reaction appears not to take place, that can mean only that it takes place too slowly for measurement or that it is reversible, the equilibrium greatly favouring the reactants. Thus the theoretical study of chemical reactions reduces simply to the problem of predicting their rates, and this in turn to predicting equilibria of reversible reactions; for the rate of a reaction is determined by the equilibrium between the reactants and the transition state (p. 28).

Now any equilibrium is governed by the differences in entropy and heat-content between the reactants and products; and so our problem becomes the prediction of such entropy and energy differences. In particular, the equilibrium concentration of the transition complex in a reaction, and consequently the rate of reaction, will be increased by an increase in the entropy of activation or a decrease in the activation energy.

Entropy of activation

The entropy of a molecule is a function of its modes of vibration and rotation as a whole, and is not determined in any simple or additive way by the bonds in it. It is possible to calculate the entropies of a few simple molecules and also the entropies of a few simple transition complexes (assuming in the latter case a plausible configuration for the complex); but the entropy of molecules cannot as a rule be theoretically predicted. Hence we are forced to assume that differences in entropy of activation play a negligible part in determining reaction rates—i.e. that rates differ only because the activation energies differ. This is the basic assumption of the electronic theory of reaction rates, and it is amply justified by the success of the theory. The main exceptions to the rule can be classed under the general heading of steric hindrance; steric factors may lower the probability of energy-rich reactant molecules reacting, that is, they may lower the entropy of activation by reducing the effective degrees of freedom of the transition complex. This phenomenon is of course well known in organic chemistry and later we shall encounter a number of examples; but in the majority of 'unhindered' reactions the assumption that activation entropy is constant seems to be a sufficient approximation.

Activation energy

It is at present quite impracticable to calculate the absolute activation energies of even the simplest reactions, except in the crudest manner. Therefore we are reduced to seeking qualitative principles which will at least enable us to predict the relative activation energies and so the relative rates of different reactions. We may for convenience divide the activation energy into three parts; representing differences in bond-energy,† in resonance energy, and in electronic binding energy† between the reactants and the transition state.

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† Since we assume that the activation entropy is constant, we may ignore the distinction between bond-energy and binding energy.

1. *Bond-energy differences*

These can be of two kinds. Firstly, bonds that are formed or broken during the reaction will be partly formed or partly broken in the transition state. (We may conveniently write formulae for transition states with such bonds denoted by dotted lines.) Since the bond-energies of such partial bonds differ from the bond-energies of corresponding full bonds, the total bond energy of the reactants will differ from that of the transition state.

Secondly, the transition state differs from the reactants in its electron configuration and stereochemical structure; such a difference may affect the bond-energies of bonds not directly taking part in the reaction. This is obviously a second-order effect and we may neglect it; indeed, we must do so since the resulting changes in bond-energy cannot be predicted. Our only concession will be to admit that there may be more or less steric strain in the reactants than in the transition state, as in a reaction leading to the formation of a 4-membered ring; but we regard such effects of strain as features of special reactions only, and ignore them in 'strainless' reactions.

2. *Resonance-energy differences*

If the initial and transition states of a reaction differ in resonance energy, the activation energy will be correspondingly affected. Now the transition state generally has a configuration, and so a resonance energy, intermediate between that of the reactants and products. Hence if a reaction involves an increase in resonance energy, the transition state will usually have a higher resonance energy than the reactants; the overall activation energy will therefore be less than in a corresponding reaction where neither reactants nor products are mesomeric, and so the former reaction will occur the more readily. Conversely a reaction involving a decrease in resonance energy will occur less readily.

It is important to remember that the transition state may have a structure which differs qualitatively from either the reactants or the products. It is then possible for the transition state to be mesomeric although neither reactants nor products are, and any such mesomerism will facilitate the reaction. A good example is the easy bimolecular hydrolysis of α-chloroketones (p. 73).

3. *Differences in electronic binding energy*

By this we mean differences in energy due to the transfer of net charge during ionic reactions. In radical reactions the effect is generally unimportant. In a simple ionic reaction, the anionoid reagent effectively loses an electron, the cationoid reagent effectively gains one. Now the energy required to remove an electron from an atom or group is called its

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† This term is defined below.

ionization potential; the energy liberated by union of the atom or group with an electron is called its *electron affinity*. The charge transfer in an ionic reaction will then lead to a decrease in energy ΔE given by

$$\Delta E = A - I,$$

where A is the electron affinity of the cationoid reagent, I the ionization potential of the anionoid reagent.

In the transition state there will be only a partial displacement of charge; if this displacement is a fraction ϵ of the electronic charge, the corresponding energy difference will be δE, given by

$$\delta E = \epsilon \Delta E = \epsilon(A - I).$$

Since the activation energy will be decreased by an increase in δE, reaction will occur more readily, the larger A or the smaller I. This confirms our definition of anionoid reagents as electron donors and of cationoid reagents as electron acceptors; for the smaller the ionization potential (I) of an anionoid reagent, the more readily it will give up an electron; and the larger the electron affinity (A) of a cationoid reagent, the more readily it will accept one.

Application of the general principles

The best way to show how these arguments are applied to the study of reaction rates seems to be by example rather than by abstract discussion. The following are a series of simple reactions where one or other of the three effects is of paramount importance.

1. *Bond-energy effects*

In the simple radical replacement reaction between sodium vapour and a methyl halide, by which sodium halide and a methyl radical are formed,

$$\mathrm{Na} + \mathrm{X{-}CH_3} \rightarrow \mathrm{NaX} + \cdot\mathrm{CH_3},$$

there is no charge displacement† and no change in resonance energy. The activation energy of the reaction should therefore be mainly determined by bond-energy changes.

The energy difference ΔE between the reactants and the transition state may be written

$$\Delta E = E'_{\mathrm{NaX}} + E'_{\mathrm{CX}} - E_{\mathrm{CX}},$$

where E_{CX} is the normal CX bond-energy, E'_{NaX}, E'_{CX} the bond-energies of the partial bonds in the transition state. Now in a series of such closely related reactions it is reasonable to suppose that the transition-state bonds will have bond-energies which are constant fractions of the normal bond-energies. Moreover, the NaX bond-energies are probably much the same since the sodium halides are highly polar and the bond-energies are largely electrostatic. We then have

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† The fact that the NaX bond in the product is highly polar is irrelevant; the molecule NaX is neutral as a whole.

$$\Delta E = A+B.E_{\mathrm{CX}},$$

where A, B are constants. Therefore ΔE should be smaller, and so the activation energy less, the smaller E_{CX}. In Table 10 activation energies for reaction of the methyl halides with sodium are given,† together with values for the corresponding C—halogen bond-energies. It will be seen that the activation and bond-energies fall together as our discussion requires.

TABLE 10

X	*Activation energy* $\mathrm{Na + MeX \rightarrow NaX + Me}$	C—X *bond-energy*
F	>25·0 Cals.	118·3 Cals.
Cl	9·7 ,,	77·8 ,,
Br	5·0 ,,	65·3 ,,
I	2·5 ,,	56·8 ,,

2. *Effect of resonance energy*

Allyl chloride is not mesomeric, unlike the allyl radical formed by reaction with sodium vapour. In the transition state of this reaction, the nascent allyl radical is also mesomeric; the activation energy is thus correspondingly reduced in comparison with similar reactions of saturated primary chlorides (Table 11). The reactions of benzyl and cinnamyl chlorides are similar; here the reactants are also mesomeric, but there is nevertheless an increase in activation energy during reaction, the benzyl and cinnamyl radicals having larger resonance energies than the parent chlorides.

TABLE 11

R	*Activation energy*† $\mathrm{Na + RCl \rightarrow NaCl + R}$
Et— . . .	9·7 Cals.
$\mathrm{CH_2{=}CH{\cdot}CH_2}$— .	5·3 ,,
$\mathrm{Ph{\cdot}CH_2}$— . .	2·5 ,,
$\mathrm{Ph{\cdot}CH{=}CH{\cdot}CH_2}$—	2·0 ,,
$\mathrm{CH_2{=}CH{\cdot}}$ . .	10·1 ,,
Ph· . . .	10·2 ,,

On the other hand, vinyl chloride is mesomeric, but the vinyl radical is not; hence reaction with sodium involves a decrease in resonance energy and consequently reaction occurs less readily than in the case of a saturated chloride. Chlorobenzene is analogous since the phenyl radical has a smaller resonance energy than the chloride.

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† Hartel and Polanyi, *Z. phys. Chem.* 1930, B **11**, 97; Hartel, Meer, and Polanyi, ibid. 1932, B **19**, 139; Frommer and Polanyi, *Trans. Faraday Soc.* 1934, **30**, 519; Haresnape, Stevels, and Warhurst, ibid. 1940, **36**, 465.

3. *Effect of electron-affinity and ionization potential*

In the ionic replacement reaction

$$X^- + CH_3—Y \rightarrow X—CH_3 + Y^-$$

the contribution to the total activation energy due to charge transfer will be (p. 48) given by

$$-\delta E = \epsilon(A_Y - I_X),$$

where A_Y, I_X are respectively the electron-affinity of Y and the ionization potential of X; and ϵ, the fractional charge transfer in the transition state, should be roughly constant for a series of similar reactions.

Therefore such replacements should occur more readily, other things being equal, the greater A_Y and the smaller I_X. Now electron-affinity rises in the series $NH_2 < OH <$ halogen; it is therefore easy to see why halogens in methyl halides replace readily, although hydroxyl and amino in methanol and methylamine do not. Moreover, in cases where activated hydroxyl or amino groups undergo replacement, amino always replaces less readily than hydroxyl. Further, removal of a second electron from an atom naturally requires more energy than removal of the first, since the second electron must be removed from a positive ion; therefore positively charged oxygen and nitrogen in 'onium salts have higher electron-affinities than the uncharged atoms in alcohols and amines. Consequently replacement occurs readily in oxonium and ammonium ions, oxonium again reacting the more readily (since in similar compounds oxygen always has a higher electron-affinity than nitrogen).

Conversely the ionization potential of a negative ion is less than that of a corresponding neutral molecule. Hence alkyl halides react more readily with OH^- ions than with neutral water.

It should be added that bond-energy effects are also important in these reactions; thus the methyl halides react in the order

$$MeF < MeCl < MeBr < MeI,$$

although the electron-affinities fall in the series $F > Cl > Br > I$. Here the dominant effect is the decrease in C—halogen bond-energy along the series. However, the fact that methyl fluoride replaces more readily than does methanol cannot be so explained since the C—O and C—F bond-energies are comparable; here differences in electron-affinity must control the reactivity.

Effect of substituents

Having outlined the general theory of reaction rates, the next problem must be to determine the effect of structural changes on the rate of a given reaction, that is, the effect on the reaction rate when hydrogen in one of the reactants is replaced by some substituent. The effects of substituents may again be divided into three categories: effects on the bond-energy, electronic binding energy, and resonance energy of activation.

1. *Effect on bond-energy*

A substituent may alter the bond-energies of other bonds in a molecule or it may alter the energies of the partial bonds present in the transition state of a reaction. Ideally, of course, these bond-energy changes should be predictable by exact calculation, but as usual the mathematical difficulties are at present quite insuperable. However, such energy changes are due entirely to changes in electron-distribution; and as such we may classify them under the headings of changes in electronic binding energy or changes in resonance energy. The only true bond-energy effect that we must admit into our treatment is that due to steric strain. Thus the stability of the coordination complexes (I, p. 43), formed by union of amines and trialkylborons, decreases with size and number of the substituents;† this effect is undoubtedly due to steric repulsion of the groups attached to nitrogen and boron.

Again, the ready dissociation of hexa-*o*-tolylethane into free radicals (p. 244) is probably due largely to a similar steric strain (or steric hindrance) effect. But just as the energy of a mesomeric molecule may be subdivided into a normal bond-energy contribution *plus* an additional resonance energy, so the energy of a hindered molecule may be regarded as a normal bond-energy sum *minus* a steric strain energy. Therefore we assume that substituents do not affect the normal bond-energy of a molecule but that they may add or subtract supernumerary forms of energy; these in turn may be electronic (resonance energy or electronic binding energy) or structural (steric strain). And in the same way that we neglect entropy changes in general, but make a special allowance in cases of steric hindrance where the effective collision frequency (and hence the entropy of activation) are reduced, so also we ignore bond-energy changes due to substituents, but make a special allowance for steric strain when steric hindrance is obviously involved.

2. *Effect on electronic binding energy: inductive effect*

A negative charge reduces the electron-affinity and ionization potential of an atom; thus it increases its anionoid activity and reduces its cationoid activity. A substituent which produces a partial negative charge on an adjacent atom will therefore increase the anionoid activity of that atom and reduce its cationoid activity. Clearly a partial positive charge will have the opposite effect.

If hydrogen in a molecule XH is replaced by a substituent Y, the polarities of the XH and XY bonds will generally differ. Therefore X in XY will be either more positive or more negative than X in XH. This difference will be reflected in the dipole moments of the XH and XY bonds, the charge displacement δe in each case being given by

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† Brown, *J.A.C.S.* 1945, **67**, 374, 378.

$$\delta e = \frac{\mu}{a},$$

where μ is the dipole moment and a the length of the bond.

Substituents can therefore be divided into two classes; those which 'induce' a negative charge on an adjacent atom when they replace hydrogen, and those which 'induce' a positive charge.

Those which induce a negative charge will increase the anionoid activity of the adjacent atom, those which induce a positive charge will increase the cationoid activity. This polarity effect is called the *inductive effect*, and it was established by organic chemists before bond-polarities had been measured. Needless to say, such measurements have entirely confirmed the existence and sign of the electron displacements which organic chemists had postulated. Substituents are classified under this heading as anionoid (or negative) inductive and cationoid (or positive) inductive in type; the former inducing negative, the latter positive, charges on adjacent atoms. These terms are conveniently abbreviated† to −I (anionoid) and +I (cationoid).

The inductive effect of a substituent is indicated by an arrow showing the direction of electron-drift (cf. notation for polar bonds, p. 37). It should be remembered, however, that the inductive effect refers to the polarity relative to a corresponding bond with hydrogen. Thus methyl is a −I substituent, and if we were treating ethane as a methylmethane we should write it as

$$\mathrm{Me{\rightarrow}CH_3}.$$

Of course the C—C bond is (absolutely) non-polar; but since the C—H bond is polar, with C positive,‡ the C—C bond is polar relative to the C—H bond. That is, replacement of hydrogen in methane by methyl makes the carbon more negative (or less positive, which is the same thing); hence the methyl exerts a −I effect.

The inductive effect of a substituent will naturally become more positive as the electron-affinity of the substituent increases; or to be more exact, with increase in electron-affinity of that atom in the substituent by which it is attached to the rest of the molecule. Since electron-affinity rises in the series $\mathrm{C < N < O < I < Br < Cl < F}$, +I activity rises in the series $\mathrm{CH_3 < NH_2 < OH < I < Br < Cl < F}$. The dividing line in this series comes between C and N; $\mathrm{CH_3}$ being strongly −I, $\mathrm{NH_2}$ weakly +I.

Second-order inductive effect

The activity of a substituent can in turn be varied by substitution. Thus if hydrogen in hydroxyl is replaced by a methyl group, the methyl induces a negative charge on the oxygen and so lowers its electron-affinity and hence also its +I activity. MeO is a weaker +I group than HO.

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† Many authors have used the opposite sign-convention. However, it seems more logical to class the group $\mathrm{—NMe_3^+}$ as +I rather than −I! Moreover, the convention here adopted agrees with that used by Hammett (p. 173).

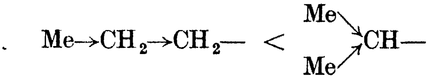
‡ Cf. Coulson, *Trans. Faraday Soc.* **1942**, **38**, 433.

If we consider a similar replacement of hydrogen in methyl by methyl, we must conclude that ethyl should be a more active —I group than methyl. Now suppose a β-hydrogen in ethyl is likewise replaced to form *n*-propyl:

$$\mathrm{Me}\rightarrow\mathrm{CH_2}\rightarrow\mathrm{CH_2}$$

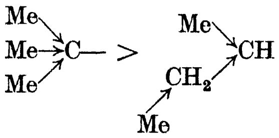
The γ-methyl induces a negative charge on the β-carbon; thus it increases the —I effect of the β-carbon compared with that in ethyl; hence the α-carbon is more negative in *n*-propyl than in ethyl and so propyl is more strongly —I than ethyl. By extending this argument it is easily seen that the inductive effect of a substituent may be relayed along a chain of atoms, just as the —I effect of the terminal methyl in *n*-propyl makes itself felt at the other end of the carbon chain.

These second-order relayed inductive effects are, however, less than the primary effects discussed in the last section. The inductive effect dies away rapidly down the chain. Therefore the effect of secondary substituents will be greater the nearer they are to the point of attachment of the primary substituent to the rest of the molecule. For instance, *iso*-propyl, or α-methylethyl, is more strongly —I than *n*-propyl (β-methylethyl):



$$\mathrm{Me}\rightarrow\mathrm{CH_2}\rightarrow\mathrm{CH_2}\text{—} < \begin{matrix}\mathrm{Me}\searrow\\ \mathrm{Me}\nearrow\end{matrix}\mathrm{CH}\text{—}$$

likewise *tert*-butyl is more strongly —I than *sec*-butyl:



$$\begin{matrix}\mathrm{Me}\searrow\\ \mathrm{Me}\rightarrow\\ \mathrm{Me}\nearrow\end{matrix}\mathrm{C}\text{—} > \begin{matrix}\mathrm{Me}\searrow\\ \mathrm{CH_2}\nearrow\\ \nearrow\\ \mathrm{Me}\end{matrix}\mathrm{CH}$$

Numerous examples of relative inductive activity will be given in the following chapters: the most striking will be found in the sections dealing with the strengths of acids and bases (p. 91).

3. *Effect on resonance energy: the electromeric* (E) *effect*

Suppose a substituent is attached to the rest of a molecule by a bond X—Y, where X is an atom in the substituent, Y one in the rest of the molecule. Then the substituent can conjugate with the rest of the molecule

(*a*) if X, Y both carry π-electrons (i.e. form parts of unsaturated systems);

(*b*) if either X or Y carries unshared *p*-electrons and the other carries π-electrons;

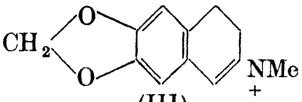
(*c*) if either X or Y has a vacant orbital and the other carries π-electrons or unshared *p*-electrons.

Examples:

(*a*) butadiene, $CH_2{=}CH{-}CH{=}CH_2$ (regarded as a substituted ethylene);

(*b*) vinyl ethyl ether: $CH_2{=}CH{-}OEt$ (regarded as a substituted ethanol);

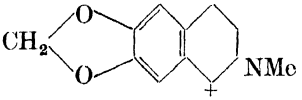
(*c*) the allyl cation: $CH_2{=}CH{-}CH_2^+$ (regarded as a substituted methyl cation). The hydrastinium cation, (III)



(III)

regarded as a substituted benzyl cation,

viz.



Substituents which influence the electronic configuration of a molecule by conjugation are said to exercise an *electromeric* (E) effect. The electromeric effect differs from the inductive effect in that electromeric substituents function only when the rest of the molecule makes the appropriate mesomerism possible.

Classification of E-substituents

Substituents in which X carries unshared p-electrons differ qualitatively from those with π-electrons; for the former cannot conjugate if Y has unshared p-electrons (but no π-electrons) while the latter can (thus hydrazine, $NH_2{-}NH_2$, is not mesomeric). Moreover, when a pair of unshared p-electrons takes part in a mesomeric system, the atom carrying them acquires a positive charge. Thus in vinyl ethyl ether complete conjugation would leave oxygen with a 1/3 share in four π-electrons, or 4/3 of a π-electron, in place of two p-electrons in the unconjugated form:

$$Et\ddot{O}{-}CH{=}CH \rightarrow Et\overset{\delta+}{O}\overset{\cdot\cdot\cdot}{-}\overbrace{CH\overset{\cdot\cdot\cdot}{-}CH_2}^{\delta-}.$$

This effect is still clearer in the hydrastinium cation (III), where 'conjugation' really amounts to the formation of a dative π-bond.

Since conjugation of a substituent with unshared p-electrons gives the substituent a positive charge, and hence the rest of the molecule a negative charge, substituents of this type will show anionoid activity. Such substituents are therefore anionoid electromeric (—E) in type.

Substituents with π-electrons can conjugate with all three types of adjacent atom—those with π-electrons, unshared p-electrons, and vacant orbitals. Taking vinyl as the substituent, the three cases are illustrated by butadiene ($CH_2\overset{\cdot\cdot\cdot}{-}CH\overset{\cdot\cdot\cdot}{-}CH\overset{\cdot\cdot\cdot}{-}CH_2$), the allyl anion ($(CH_2\overset{\cdot\cdot\cdot}{-}CH\overset{\cdot\cdot\cdot}{-}CH_2)^-$), and the allyl cation ($(CH_2\overset{\cdot\cdot\cdot}{-}CH\overset{\cdot\cdot\cdot}{-}CH_2)^+$). In the first case conjugation does not lead to charge migration; in the second, the substituent becomes more negative, the rest of the molecule more positive; in the third, the charge migration is in the opposite direction. A substituent which conjugates in all three ways, e.g. vinyl or phenyl, may be classed as ±E, since it can exert an electromeric effect of either sign according to circumstances.

Now consider a substituent of this type in which the unsaturated system contains a hetero-atom (e.g. an acyl group $R{-}\overset{|}{C}{=}O$). Hetero-atoms have larger ionization potentials and electron-affinities than carbon. If the acyl group conjugates with an empty orbital, it will become positively charged. Compared with vinyl the effective resonance energy will be less, because the resonance energy will be offset by the extra energy required to give the hetero-atom a positive charge (since its ionization potential is greater than that of carbon). Conversely, if acyl conjugates with adjacent unshared p-electrons, the oxygen becomes negative, and since hetero-atoms have larger electron affinities than carbon, the effective resonance energy is greater than in the case of vinyl. Such a substituent will therefore exert a weak $-$E effect but a strong +E effect. Moreover, if such a substituent conjugates with an unsaturated carbon chain, the high electron-affinity of the hetero-atom will enable it to acquire more than its share of the π-electrons and so to become negatively charged. Thus here again such a substituent will exert a cationoid effect.

To sum up, substituents with π-electrons, containing a hetero-atom in the unsaturated system, exert predominantly a +E effect.

Relative activities of E-substituents

(*a*) $-$E *substituents*

Since a $-$E substituent acts by acquiring a positive charge, the effect will be greater the smaller the ionization potential of the atom carrying the unshared p-electrons. Thus we have the order of $-$E activity:

$$R_2N > RO > \text{halogen}.$$

Moreover, a negative charge increases the $-$E activity:

$$RN^- > R_2N: \qquad O^- > RO.$$

Also for negative ions, the ionization potential effect operates:

$$CH_2^- > RN^- > O^-.$$

(*b*) +E *substituents*

In +E substituents increasing electron-affinity will correspondingly increase the +E activity; thus we have the order of activity:

$$-RC{=}CR_2 < -RC{=}NR < -CR{=}O.$$

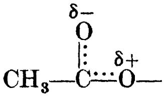
Effect of subsidiary substituents

Naturally the effect of a secondary substituent will alter the E-activity of a substituent. Thus a +I secondary substituent will effectively increase the electron-affinity and ionization potential of an E-substituent, and so increase its +E activity; and a —I secondary substituent will have the opposite effect. Consequently, —E activity increases in the series

$$HO < MeO < EtO < Pr_{\beta}O < Bu_{\gamma}O,$$

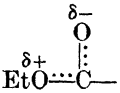
since —I activity rises in the series $H < Me < Et < Pr_{\beta} < Bu_{\gamma}$.

Likewise a secondary ±E substituent will alter the E-activity of the main substituent if the secondary substituent can conjugate with it. Thus acetoxyl is less —E than hydroxyl since conjugation of oxygen with acetyl gives the oxygen a positive charge:



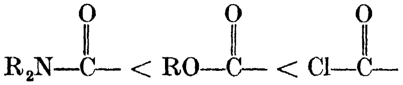
$$CH_3—\overset{\overset{\delta-}{O}}{\overset{\vdots|}{C}}\cdots\overset{\delta+}{O}—$$

while carbethoxyl is less +E than formyl since conjugation gives the carbonyl a negative charge:



$$Et\overset{\delta+}{O}\cdots\overset{\overset{\delta-}{O}}{\overset{\vdots|}{C}}—$$

Also since —E activity falls in the series $R_2N > RO > Cl$, +E activity increases in the series:



$$R_2N—\overset{\overset{O}{\|}}{C}— < RO—\overset{\overset{O}{\|}}{C}— < Cl—\overset{\overset{O}{\|}}{C}—$$

Hyperconjugation

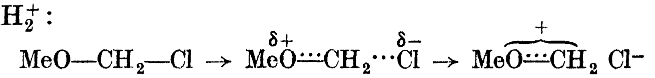
A methyl group hyperconjugates in the same way that an atom with unshared *p*-electrons conjugates. It is essentially —E in type. The two effects differ in degree though not in kind; the σ-electrons of the C—H bonds in the methyl cannot overlap so efficiently with adjacent groups as would *p*- or π-electrons. Other σ-bond electrons overlap even less efficiently than those of CH bonds; the molecular orbitals in the latter differ little from atomic orbitals since hydrogen has such a small atomic radius. Hence —E activity falls as the number of α-hydrogen atoms decreases; —E activity falls in the series $CH_3 > MeCH_2 > Me_2CH > Me_3C$.

Application to reaction theory

If a substituent conjugates more efficiently with the reactants than with the transition complex in a reaction, it will increase the activation energy and so retard the reaction; for the resonance energy due to the substituent will be less in the transition complex than in the reactants. Conversely, if a substituent conjugates more efficiently with the transition complex than with the reactants, it will facilitate reaction. Three examples will suffice for the present.

1. Methyl chloride ionizes with difficulty; but α-chloromethyl methyl ether ionizes readily. In the ether cation the methoxyl conjugates with

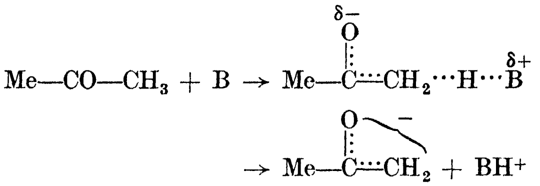
the CH_2^+; and so in the transition state the methoxyl conjugates with the nascent CH_2^+:



$$\mathrm{MeO{-}CH_2{-}Cl} \rightarrow \overset{\delta+}{\mathrm{MeO}}\mathrel{\overset{\cdots}{-}}\mathrm{CH_2}\cdots\overset{\delta-}{\mathrm{Cl}} \rightarrow \overset{+}{\mathrm{MeO}\mathrel{\overset{\cdots}{-}}\mathrm{CH_2}}\ \mathrm{Cl^-}$$

2. Benzaldehyde reacts less readily with bisulphite than does formaldehyde. In benzaldehyde the phenyl and carbonyl conjugate, but in the bisulphite addition complex no such conjugation is possible. In the transition complex, conjugation is less than in the parent aldehyde; hence reaction occurs less readily than in the case of formaldehyde where there is no conjugation.

3. Methane has no detectable tendency to react with bases. The methyl anion formed by such a reaction would not be mesomeric. Acetone is unconjugated; but the anion derived by loss of a proton is mesomeric. The transition complex is also mesomeric; thus acetone reacts with bases more readily than does methane.



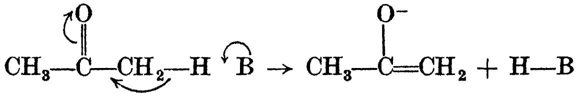
$$\mathrm{Me{-}CO{-}CH_3} + \mathrm{B} \rightarrow \mathrm{Me{-}}\overset{\overset{\delta-}{\mathrm{O}}}{\overset{\vdots}{\mathrm{C}}}\mathrel{\overset{\cdots}{-}}\mathrm{CH_2}\cdots\mathrm{H}\cdots\overset{\delta+}{\mathrm{B}}$$

$$\rightarrow \mathrm{Me{-}}\overset{\mathrm{O}^{-}}{\overset{\vdots}{\mathrm{C}}}\mathrel{\overset{\cdots}{-}}\mathrm{CH_2} + \mathrm{BH^+}$$

The anion formed by loss of H^+ from ethyl ether would not be mesomeric since in it the unshared *p*-electrons on oxygen and carbon could not conjugate. That is, the ethoxyl is a $-E$ group and in this reaction its electromeric effect is not called into play. Ether shows no detectable acidity.

Relation to the classical interpretation and symbolism

The only difference between the picture of electromeric effects given in the previous sections and that adopted in the classical theory is this: the classical theory assumed that complete transfer of pairs of electrons took place during reactions where electromeric effects are called into play; but according to the present view the transfers are only partial, the compounds involved being mesomeric, and the electrons in them therefore non-localized. Thus the reaction of acetone with bases was formerly represented:



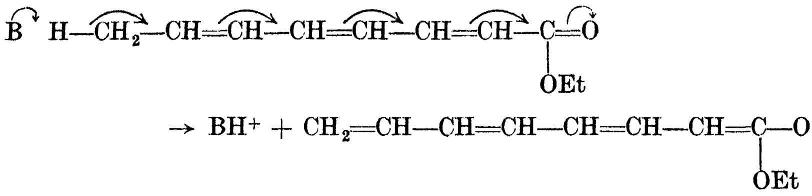
$$\mathrm{CH_3{-}}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{{-}CH_2{-}H}\ \ \mathrm{B} \rightarrow \mathrm{CH_3{-}}\overset{\mathrm{O^-}}{\overset{|}{\mathrm{C}}}\mathrm{{=}CH_2} + \mathrm{H{-}B}$$

In the present view the product does not have the negative charge confined to oxygen, but is a mesomeric compound where the negative charge is distributed over three atoms (naturally oxygen will carry more than its share of the negative charge since it has a higher electron-affinity than carbon).

The distinction is seen rather clearly in the reactions of conjugated systems. Thus the activation of methyl in esters of the type

$$\mathrm{CH_3{-}CH{=}CH{-}CH{=}CH{-}CH{=}CH{\cdot}COOEt}$$

to reaction with bases was ascribed to a transmission of the +E effect of carbonyl through the conjugated chain:



$$B\ \ H{-}CH_2{-}CH{=}CH{-}CH{=}CH{-}CH{=}CH{-}\underset{\displaystyle OEt}{C}{=}O$$

$$\rightarrow BH^+ + CH_2{=}CH{-}CH{=}CH{-}CH{=}CH{-}CH{=}\underset{\displaystyle OEt}{C}{-}O^-$$

In the present view both the initial ester and the anion are mesomeric; but the latter has the larger resonance energy both because it contains a more extended mesomeric system and because the negative charge can accumulate on the strongly electronegative oxygen.

Classical symbolism can, however, be used quite satisfactorily if its meaning is reinterpreted. An electromeric substituent acts by altering the relative resonance energies in the initial and transition states of a reaction; and as a rule the change in conjugation will involve a drift of electrons from or towards the substituent. The direction of this fractional charge displacement corresponds to that of the displacement of electron-pairs which classical electronic theory postulated, and it can be represented by the same curved-arrow symbolism. This symbolism has been used throughout, because it is both convenient and also familiar to most organic chemists.

Interaction of groups through conjugated systems, cross-conjugation

In many cases the effect of a substituent can be transmitted along a conjugated chain to a distant group. Thus the methyl groups in polyene carboxylic acid esters, $CH_3\cdot(CH{=}CH)_n\cdot COOR$, show many reactions of the methyl in corresponding acetates, $CH_3\cdot COOR$; they will, for example, undergo Claisen condensation (p. 127) with ethyl oxalate and potassium ethoxide.

Such reactions imply that groups can interact with each other through conjugated systems. Thus the acidity of methyl hydrogen in acetic esters is due to stabilization of the corresponding ester anions, $^-CH_2\cdot COOR$, by conjugation of the CH_2^- and the (+E) COOR group. If the two groups are separated by a conjugated chain, each of them will conjugate with the chain (since $\rangle C{=}C\langle$ is a ±E system and can conjugate with all types of E-substituent). It is, therefore, not surprising that E-effects of one group should influence the other.

But it is not sufficient that both groups should be attached to the same conjugated system. Thus the methyl in methacrylic esters

$$CH_2{=}CMe{-}COOR$$

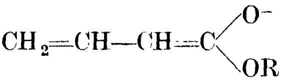
shows no appreciable acidity, although in the isomeric crotonic esters, $Me\cdot CH{=}CH\cdot COOR$, Claisen condensations take place quite readily.

Evidently the orientation of the groups determines whether they can interact.

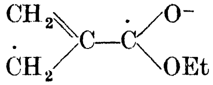
This then is the problem: two groups, X, Y, which can conjugate with each other, are attached to a conjugated system. Under what conditions will any E-effect of X influence Y? The answer can be reached in two different ways.

1. We may write the compound in resonance notation as a hybrid of several canonical forms. If one of these forms is $\overset{+}{X}=R=\overset{-}{Y}$ or $\overset{-}{X}=R=\overset{+}{Y}$, where R represents the conjugated system, and all the atoms are exerting their normal covalencies, then X, Y can interact.

Thus for crotonic ester anions we can write the form



implying that the terminal CH_2 and COOR groups can interact; but the corresponding form for the methacrylate derivative would be

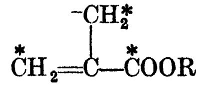


with two tervalent carbons. This diradical would have a much higher energy than the classical form $^{-}CH_2—\overset{\overset{\displaystyle CH_2}{\|}}{C}—COOR$, and so would contribute little to the actual structure of the anion; therefore the COOR group does little to stabilize the anion.

2. Coulson and Longuet-Higgins[†] have deduced a very simple rule to cover these cases, based on a detailed analysis of the molecular orbital method. The rule may be stated thus. In the formula for any conjugated compound mark alternate atoms in the mesomeric system with stars. If the starring process can be carried out so that no pair of bonded atoms are either both starred or both unstarred,[‡] then all the starred atoms will show qualitatively the same electronic behaviour and likewise all the unstarred atoms; but the starred and unstarred atoms may differ.

In the compound X—Y, X and Y can conjugate. Therefore we can at once deduce that, if in X—R—Y we carry out the starring process, starting with X*, then X, Y will affect each other only if Y is unstarred. Thus:

$$^{-}CH_2^*—CH=CH^*—COOR$$



$$\overset{*}{C}H_2=\overset{\overset{\displaystyle ^{-}CH_2^*}{|}}{C}—\overset{*}{C}OOR$$

[†] *Proc. Roy. Soc.* 1947, A **191**, 39.

[‡] This is possible in all but a few exceptional cases where odd-numbered rings are present (e.g. azulene).

Three useful conclusions follow. (*a*) If a substituent affects a reaction in a certain way, the inclusion of an unbranched chain of C=C units between the substituent and the rest of the molecule will not qualitatively alter the substituent's effect. (*b*) If a substituent has a certain effect when attached at a certain point in a conjugated system, it will have a qualitatively similar effect only at other positions which are separated from the first by an odd number of atoms. (*c*) An ion of the form $(\mathrm{C{=}C})_m\text{—}\mathrm{C}^+\text{—}(\mathrm{C{=}C})_n$ will be stablized by a $-$E substituent only if the latter is attached to an odd-numbered carbon (numbering the carbon atoms from the end of the conjugated chain). A similar rule holds for the corresponding anion and a $+$E substituent.

If, in the compound X—R—Y, the E-substituents X, Y are so placed that conjugation between them is not possible, although both are attached to the same conjugated system R, the compound is said to be *cross-conjugated.*

CHAPTER V

THE REPLACEMENT REACTION

REPLACEMENT reactions of the type $A+B—C \rightarrow AB+C$ are of especial theoretical importance because their simplicity has permitted a very thorough study† of their mechanisms. Three types are known, anionoid, cationoid, and radical replacements, of which the first are much the most important and have been investigated in far more detail than the others. All can take place by the Heitler–London mechanism; the general principles were discussed in the previous chapter. Here we shall be concerned only with the ionic replacements, radical replacements being left till later (Chapter XIII).

Anionoid replacements

These reactions are of the general type

$$\overset{-}{A} + B—C \rightarrow A—B + \overset{-}{C},$$

where $\overset{-}{A}$ is an anionoid reagent containing an unshared pair of electrons which bond A to B in the product. In the initial state either A or C may carry electric charges; several different charge-types are therefore possible, but the mechanism is similar in each case. Examples of the different possibilities are:

(*a*) A, C uncharged initially:

$$R_3N + Me—I \rightarrow R_3N^{+}—Me \quad I^{-}.$$

(*b*) A^{-}, C uncharged:

$$HO^{-} \quad Me—I \rightarrow HO—Me \quad I^{-}.$$

(*c*) A uncharged, C^{+}. This type has not been observed.

(*d*) A^{-}, C^{+}:

$$HO^{-} \quad Me—\overset{+}{S}Me_2 \rightarrow HO—Me \quad SMe_2.$$

Kinetic studies have shown that all these reactions can be divided into two distinct types. Reactions of the first type are bimolecular, their rates depending on the concentrations of both reactants (A and BC), while reactions of the other type are unimolecular and their rates depend only on the concentration of the BC reactant. Thus the rate of hydrolysis of methyl bromide by alkali in aqueous alcohol is proportional to the concentrations of both alkali and halide, while the rate of hydrolysis of *tert*-butyl bromide under the same conditions is independent of the concentration of alkali. Hughes and Ingold have termed the bimolecular reactions S_2, the unimolecular S_1, and these terms have been generally adopted.

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† Much of the work in this field has been carried out by Hughes and Ingold and their collaborators, and has been well summarized in a discussion, *Trans. Faraday Soc.* 1941, **37**, 603.

It is clear that S_2 replacements may take place by the adiabatic Heitler–London mechanism, but that the S_1 replacements must take place in at least two stages. The rate-determining step in an S_1 replacement involves only one of the reactants (see p. 21).

The S_2 mechanism

An examination of the stereochemistry of the reactants and products has shown that the S_2 reactions do follow the Heitler–London mechanism. It has long been known that replacements may lead to a change in configuration, that is, if B is an asymmetric carbon atom, the product AB may have the opposite configuration to BC. It is indeed very difficult to establish that inversion does occur in a given replacement. We can show, and Walden did show, that by a series of successive replacements a compound BC can be converted into its antipode, but this only tells us that an odd number of the replacements have taken place with inversion, and the configurations in the intermediate steps cannot so be ascertained. The situation was also confused by the fact that other replacements may take place with racemization or even retention of configuration.

Kenyon, Phillips, and their collaborators† were able to find a reaction where complete inversion demonstrably took place. They carried out the following series of conversions with a number of active alcohols:

$$\begin{tikzcd}
(+)\ R_1R_2R_3C\text{—}OH \arrow[r, "PhSO_2Cl"'] & (+)\ R_1R_2R_3C\text{—}OSO_2Ph \arrow[d, "NaOAc"] \\
(-)\ R_1R_2R_3C\text{—}OH & (-)\ R_1R_2R_3C\text{—}OAc \arrow[l, "OH^-"']
\end{tikzcd}$$

In the first reaction it is the hydrogen of the hydroxyl which is replaced by benzenesulphonyl; the C—O bond remains intact and the product must have the same configuration as the alcohol. Also it is known from other evidence (p. 118) that in the hydrolysis of esters of carboxylic acids it is the CO—O bond which breaks; the alcohol must therefore have the same configuration as the ester. Therefore the third reaction in the cycle (hydrolysis of the acetate) must also take place without change in configuration. Since the whole reaction involves inversion, the product being almost 100 per cent. optically pure, the second reaction must take place with inversion. Other evidence (p. 123) shows that in the hydrolysis of alkyl benzene-sulphonates it is the alkyl—O bond which breaks and so inversion might well occur. Further, such reactions are known to be bimolecular, suggesting that bimolecular S_2 reactions in general may lead to inversion.

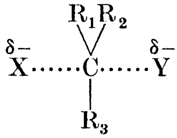
This conclusion was confirmed by Hughes and Ingold and their collaborators,‡ who found that in the alkaline hydrolysis of a series of optically active halides to alcohols, the S_2 mechanism leads to complete inversion.

† *J.C.S.* 1923, **123**, 44; 1925, **127**, 399, 2552; 1926, 2052; 1933, 173; 1935, 1072, 1663; 1936, 303.

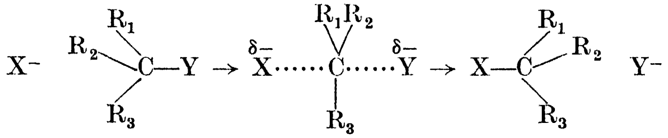
‡ Summarized by Cowdray, Hughes, Ingold, Masterman, and Scott, *J.C.S.* 1937, 1252.

This conclusion was further proved by use of radioactive indicators.† When an optically active iodide is treated with iodide ion in acetone it racemizes. An S_2 replacement by iodide ion leads to the optical antipode of the initial iodide. Naturally it is impossible to measure the rate of replacement by normal methods, but if the racemization is carried out with radioactive iodide ion, the rate of replacement can be determined from the rate at which the alkyl iodide becomes radioactive. Using *sec*-octyl iodide it was found that the replacement reaction was bimolecular and that the rates of replacement and racemization were the same. Therefore every reaction of iodide ion with octyl iodide leads to inversion.

Now this inversion of configuration is difficult to interpret in classical terms; but as Olson‡ and Meer and Polanyi§ pointed out, inversion would be expected if the Heitler–London mechanism were operative. In the transition state of such a reaction, $X^- + R_1R_2R_3C—Y \rightarrow X—CR_1R_2R_3 + Y^-$, X and Y would be both bonded to the central carbon: and having like charges they should tend to lie in line with it. The three alkyl groups will then presumably lie in a plane with the carbon atom, the plane lying perpendicular to the X—C—Y line, thus:

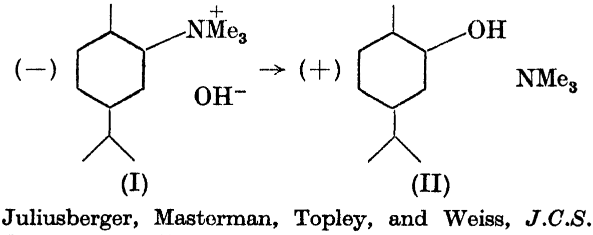


When Y separates as an ion, the carbon returns to its normal tetrahedral configuration, but this configuration is the mirror image of the initial configuration of $R_1R_2R_3C—Y$, thus:



The fact that inversion does accompany S_2 replacements is therefore a strong indication that they do take place by the Heitler–London mechanism.

It may be added that it is not merely electrostatic repulsions in the transition state that keep X, C, and Y in line. Read and Walker‖ have shown that the decomposition of *l*-piperityltrimethylammonium hydroxide (I) gives *d*-piperitol (II), inversion taking place,



(I) (II)

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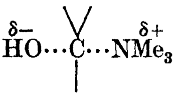
† Hughes, Juliusberger, Masterman, Topley, and Weiss, *J.C.S.* 1935, 1525; Hughes, Juliusberger, Scott, Topley, and Weiss, ibid. 1936, 1173; Cowdrey, Hughes, Nevell, and Wilson, ibid. 1938, 209.

‡ *J. Chem. Phys.* 1933, **1**, 418.

§ *Z. phys. Chem.* 1932, B **19**, 164.

‖ *J.C.S.* 1934, 308.

although in the transition state the hydroxyl and amino groups have opposite charges and should attract one another.



$$\overset{\delta-}{HO}\cdots C\cdots \overset{\delta+}{NMe_3}$$

Evidently the configuration of the transition state is determined by definite covalency forces, and it is interesting that the configuration is the same trigonal bipyramidal one that one finds in phosphorus pentahalides in the vapour phase. This conclusion has been further confirmed by recent work on the hydrolysis of neopentyl halides (p. 76).

The S_1 mechanism

When optically active alkyl halides react with anionoid reagents by the S_1 mechanism, the products are partly racemized, but the inverted product predominates. The mechanism of this reaction must therefore differ from that of the S_2 replacement. In any case the kinetic evidence proves that the reaction must take place in at least two stages, the rate-determining step involving one reactant only. It was suggested by Ward,† by Norris and Banta,‡ and by Gleave, Hughes, and Ingold§ that this step is an ionization of the halide to form a carbonium ion; the ion then rapidly condenses with the anionoid reagent to form the final product.

$$R{-}X \rightarrow R^+ \quad X^-$$
$$R^+ + A^- \rightarrow R{-}A.$$

Since carbonium ions are planar, having the same sp_2 hybridized structure as free methyl or tervalent boron (p. 7), the intermediate ion will be symmetrical and the reaction should lead to racemization; but if the second step takes place very rapidly, it will occur before the R^+ and X^- ions have time to separate, and the X^- ion will shield one side of the R^+ ion so that attack by A^- will take place preferentially from the opposite side. The reaction should therefore lead to partial inversion with racemization, as is in fact the case.

The ionization mechanism is supported by two lines of evidence. Firstly, certain alkyl halides racemize in liquid sulphur dioxide solution at a rate which is independent of the halide ion concentration in the solvent,‖ that is, by an S_1 mechanism, and Tuck†† has also shown that *tert*-butyl iodide exchanges iodine with radioactive iodide ion in the same solvent by a unimolecular process. Liquid sulphur dioxide is an excellent ionizing solvent and it is difficult to see any reasonable mechanism, other than ionization, for these reactions.

$$R{-}I \rightarrow R^+ \quad I^-$$
$$R^+ + I^- \rightarrow RI.$$

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† *J.C.S.* 1927, 2285. ‡ *J.A.C.S.* 1928, **50**, 1804. § *J.C.S.* 1935, 236.

‖ Bergman and Polanyi, *Naturwiss.* 1933, **21**, 378; Szabo, *Diss.*, Berlin, 1933.

†† *Trans. Faraday Soc.* 1938, **34**, 222.

Secondly, Bateman, Church, Hughes, Ingold, and Taher[†] have found that in the S_1 hydrolysis of benzhydryl chlorides in aqueous alcohol the rate of reaction decreases as the reaction proceeds.

$$Ph_2CH—Cl \rightarrow Ph_2CH^+ \quad Cl^-$$
$$Ph_2CH^+ + H_2O \rightarrow Ph_2CHOH_2^+$$

This effect would be expected if ionization were one of the reactions involved, since the intermediate carbonium ion may react with chloride ion to regenerate the starting material; as the concentration of chloride ion increases during the reaction, a progressively larger fraction of the carbonium ions formed react with it to regenerate benzhydryl chloride and so the rate of hydrolysis falls.

On the other hand, Lucas and Hammett[‡] have found that the S_1 hydrolysis of *tert*-butyl nitrate is accelerated by perchlorates, but retarded by other anions including hydroxyl. Now an ionization should be facilitated by any increase in the ionic strength of the solvent, and so they conclude that the reaction is really pseudo-unimolecular and takes place through an attack by solvent on the halide. The concentration of the solvent will be involved in the rate expression, but since it will remain sensibly constant during reaction, the reactions are apparently of first order. Salts will, however, reduce the activity of the solvent and so decrease the rate of reaction. They suggested that the effects observed by Hughes, Ingold, and their collaborators might be explained in this way.

There is no doubt that the solvent plays a part in the reaction since S_1 mechanisms are not observed in the vapour phase. One important effect of a solvent on an ionization would be a reduction of the interionic forces by virtue of its dielectric properties. It is true that S_1 reactions take place more readily in solvents of high dielectric constant (*vide* p. 76), but this is not the whole story. Various authors[§] have found that the solvolysis of benzhydryl chloride in alcohol is greatly accelerated by small amounts of water, and of course similar differences between reaction rates in dry and moist solvents have long been known qualitatively to organic chemists. The effects are much too great to be ascribed to any change in the dielectric constant. Nor can the water be reacting by an S_2 mechanism with the halide, since the product in moist alcohol is still benzhydryl ethyl ether. The only reasonable explanation is that water has a more powerful affinity for chloride ion than alcohol and so facilitates ionization of the benzhydryl chloride; the benzhydryl ion then reacts indiscriminately with a molecule of solvent and since alcohol is present in excess, the main product is the ether.

$$Ph_2CH—Cl + H_2O \rightarrow Ph_2CH^+ \; (Cl \cdots OH_2)^-$$
$$Ph_2CH^+ + EtOH \rightarrow Ph_2CH—OEt + H^+$$

The energy required to ionize an alkyl halide in a vacuum would be extremely great. The driving force of the S_1 ionization must be a solvation of the resulting ions. It is meaningless to talk of bulk dielectric constants of solvents when one is discussing systems of the same size as the solvent molecules. The solvent stabilizes ions because molecules of solvent are electrostatically attracted to them and the stabilization will depend on the total electrostatic energy of the shell of solvent molecules surrounding the ion. If we introduce a small amount of a second solvent whose molecules are bound more firmly by ions, it may stabilize the ions to a quite disproportionate extent; the ions will tend to surround themselves with a sheath of the foreign molecules even though the concentration of the latter may be small. The ionization of an alkyl halide may then be written

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[†] *J.C.S.* 1940, 960, 966, 971, 974, 979.

[‡] *J.A.C.S.* 1942, **64**, 1928.

[§] See Farinacci, Steigman, and Hammett, ibid. 1937, **59**, 2536, 2542.

$$\mathrm{S}\quad \mathrm{R—X}\quad \mathrm{S} \rightarrow (\mathrm{S}\cdots\mathrm{R})^{+}\quad (\mathrm{X}\cdots\mathrm{S})^{-},$$

where S represents a number of molecules of solvent. The transition state will be

$$\overbrace{\mathrm{S}\cdots\mathrm{R}}^{\delta+}\cdots\overbrace{\mathrm{X}\cdots\mathrm{S}}^{\delta-}$$

and the energy will be lowered by the energy of solvation of the nascent ions. Now the attachment of the solvent molecule to the ions will be accompanied by a distortion of their electronic orbitals and a large decrease in energy; the process is altogether analogous to the formation of a covalent bond. Therefore the S_1 ionization is really completely analogous to an S_2 replacement except that the ionic 'products' contain electrostatic bonds, and not covalent links. The ionization should proceed through a definite transition state and its rate should therefore be governed by the general principles laid down in the previous chapter. In practice it is convenient to omit the solvent in writing formulae for S_1 reaction intermediates, but it is important to remember that the distinction between S_1 and S_2 reactions is not fundamental.

Requirements for anionoid replacements

For the energy of the transition state $\overset{\delta-}{\mathrm{A}}\cdots\mathrm{B}\cdots\overset{\delta-}{\mathrm{C}}$ to be reasonably low, that is, for the activation energy of the replacement reaction

$$\mathrm{A}^{-} + \mathrm{BC} \rightarrow \mathrm{AB} + \mathrm{C}^{-}$$

to be small and its rate high, three general conditions must be fulfilled. Firstly, the energies of the AB and BC bonds in the transition state should be as high as possible. Secondly, since in forming the transition state electrons move from A to C, the electron-affinity of C should be as high and that of A as low as possible; and thirdly, the resonance energy of the transition state should be as high, that of the initial state as low, as possible.

The classification of anionoid reagents in terms of the electron-affinity of the central atoms in them have been discussed and need not be recapitulated. Changes in the electron-affinity of C have the opposite effect. Thus replacement occurs with diminishing ease in the series

$$\text{halogen} > \mathrm{O} > \mathrm{N} > \mathrm{C}$$

when the central atom of C (in the reaction $\mathrm{A}^{-}+\mathrm{BC}\rightarrow\mathrm{AB}+\mathrm{C}^{-}$) is

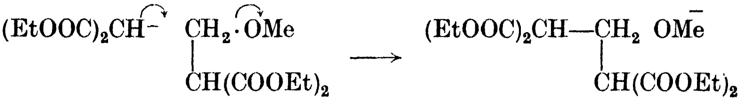
C, N, O, or halogen. If B is carbon, replacement occurs readily if C is halogen but only in special cases if C is oxygen, carbon, or nitrogen. In these special cases ease of reaction falls in the series O > N > C. If the electron-affinity of C is raised by 'onium salt formation, the rate of reaction increases; thus the hydroxyl in alcohols can be replaced by halogen by treatment with hydrogen halides; the reaction undoubtedly takes place through an intermediate 'onium salt,

$$\mathrm{R{-}OH + HX \rightarrow ROH_2^+\ X^-}$$

$$\mathrm{X^-\ R{-}\overset{+}{O}H_2 \rightarrow X{-}R\ \ OH_2}$$

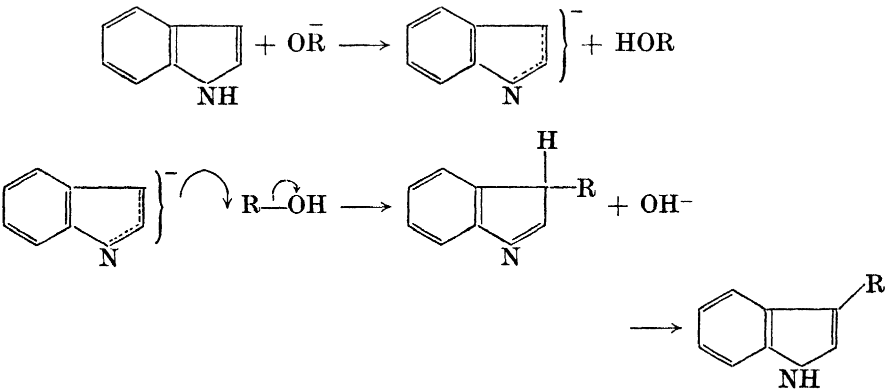
where salt formation has increased the electron-affinity of oxygen. Similar reactions take place, though less readily, with quaternary ammonium salts and anionoid reagents.

(There are one or two reactions where neutral hydroxyl or alkoxyl groups apparently undergo replacement—a possibility which does not seem to have been considered. A simple case is the condensation of malonic ester in presence of bases with methoxymethylmalonic ester:



$$\mathrm{(EtOOC)_2CH^-\ \ \underset{CH(COOEt)_2}{CH_2\cdot OMe} \longrightarrow (EtOOC)_2CH{-}\underset{CH(COOEt)_2}{CH_2}\ \ O\bar{M}e}$$

other related reactions are the alkylation of indoles by sodium alkoxides in alcohols under drastic conditions,† and the similar well-known alkylations of pyrroles. The most likely mechanism is



The corresponding alkyl halides react readily in the cold with metal derivatives of pyrrole or indole. It is interesting that the ease of replacement with alcohols falls in the series Me > Et > Pr_β > Bu_γ, *tert*-butyl alcohol not reacting; this order of reactivity would be expected in an S_2 replacement, p. 70.)

The effective strength of the BC bond in the transition state can be altered in two ways. Firstly, in related reactions, where the strength of the bond should be a more or less constant fraction of the initial BC bond-energy, the effective strength will increase as the BC bond-energy decreases ; for the total bond-energy e_0 of the transition state relative to the initial state will be given by

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† Cornforth and Robinson, *J.C.S.* 1942, 680.

$$e_0 = (1-\alpha)e_1-\beta e_2,$$

where e_1, e_2 are the BC and AB bond-energies, and α, β the fraction of their total bond-energies that the bonds BC and AB have in the transition state. Therefore the smaller e_1, the smaller e_0, and the smaller the activation energy of the reaction. This effect is seen in the reactions of alkyl halides, the reactivity falling in the series $RI > RBr > RCl > RF$, while the bond-energies rise in the series $CI < CBr < CCl < CF$.

Secondly, the effective bond-energy can be altered by changing α in the above expression for e_0. The larger α, the smaller the transition state energy. This raises a most interesting point. If we consider two successive replacements

$$B^- + C{-}D \rightarrow B{-}C + D^-$$

$$A^- + B{-}C \rightarrow A{-}B + C^-$$

it is reasonable to suppose that the BC bonds in the transition states

$$\overset{\delta-}{B}\cdots C\cdots\overset{\delta-}{D} \qquad \overset{\delta-}{A}\cdots B\cdots\overset{\delta-}{C}$$

should have very similar energies ; that is, the value of β in the expression for the energy of the first transition step should be the same as that of α in the second. Consequently a group which in such transition states forms bonds which have a large fraction of the total bond-energy, will be both an effective anionoid reagent and an effective replaceable group. It is difficult to predict how this fraction will vary with the structure of the group, but we may expect it to increase with the deformability of the central atom. If so, the iodide ion should be particularly effective. It might then be possible for a replacement reaction

$$A^- + B{-}C \rightarrow A{-}B + C^-$$

to take place more readily in presence of iodide ions by the two steps,

$$I^- + B{-}C \rightarrow I{-}B + C^-$$

$$A^- + B{-}I \rightarrow A{-}B + I^-$$

the iodide ion being a better anionoid reagent than A^- and the iodine atom a better replaceable group than C. This is undoubtedly the reason why iodide acts as a catalyst in many such replacements. Thus the reactions

$$MeBr + I^- \rightarrow MeI + Br^-$$

$$MeI + OH^- \rightarrow MeOH + I^-$$

are both much faster than the one-step hydrolysis

$$MeBr + OH^- \rightarrow MeOH + Br^-$$

and therefore iodides catalyse the hydrolysis of methyl bromide.

So far only S_2 anionoid replacements have been discussed, but the same considerations apply to S_1 replacements. The rate-determining step of an S_1 replacement $A^- + BC \rightarrow AB + C^-$ is an ionization of the molecule BC. Written in full this reaction is

$$\mathrm{BC}\ (+\ \mathrm{S}) \rightarrow \overbrace{\mathrm{S\cdots B}}^{\delta+}\cdots\overbrace{\mathrm{C\cdots S}}^{\delta-} \rightarrow (\mathrm{S\cdots B})^+\ (\mathrm{C\cdots S})^-$$

where S represents several molecules of solvent. The energy of solvation of the ions in the final and transition states will be largely independent of their nature, since the forces involved are electrostatic. The energy of ionization will be

$$(1-\alpha)e_1 - e_5 + e_3 - e_4,$$

where e_5 is the (constant) energy of solvation of the nascent ions, e_1 is the BC bond-energy in the initial state, αe_1 its energy in the transition state, e_3 the ionization potential of B, e_4 the electron-affinity of C. The activation energy of the reaction will therefore be smaller, the smaller e_1 or the greater α, just as in S_2 replacements. The difference $(e_3 - e_4)$ is the energy required to transfer an electron from B to C and will be smaller, the smaller e_3 or the greater e_4; therefore the activation energy will be less, the smaller the ionization potential of B or the larger the electron-affinity of C. Therefore the only difference between the rates of S_1 and S_2 reactions are that only the former depend on the ionization potential of B, only the latter on the anionoid reactivity of A^-. We shall return to this point later.

Effect of substituents

1. —S_1 *replacements*

The rate-determining step in the S_1 replacement $A^- + B—C \rightarrow A—B + C^-$ is the ionization of BC. In the corresponding transition state B has a partial positive charge and a partially vacant orbital while C has a partial negative charge and a pair of electrons partly unshared:

$$\mathrm{B—C} \rightarrow \overset{\delta+}{\mathrm{B}}\cdots\overset{\delta-}{\mathrm{C}}.$$

A —E substituent in A or a +E substituent in C will then be able to conjugate with B or C in the transition state and so facilitate ionization. A +E substituent in B or a —E substituent in C will have little effect on the reaction rate since their electromeric effects will not be called into play.

The effect of inductive substituents can also be predicted from a consideration of the nature of the inductive effect.

A +I substituent in B will induce a positive charge in B. It will therefore strengthen B's hold on the B—C bond electrons and so increase the energy required for C to separate as an anion. Conversely, a —I substituent in B should facilitate the ionization of C. Thus +I substituents in B should retard, —I facilitate the S_1 replacement. Clearly substituents in C will have the opposite effect, +I facilitating and —I retarding the ionization of BC.

EXAMPLES

1. Methyl chloride has never been observed to undergo a $-S_1$ replacement; but introduction of $-E$ methoxyl gives α-chlorodimethyl ether which hydrolyses readily by the $-S_1$ mechanism:

$$\mathrm{MeO}\overset{\curvearrowright}{—}\mathrm{CH_2}\overset{\curvearrowright}{—}\mathrm{Cl} \rightarrow \overset{+}{\overbrace{\mathrm{MeO}\mathrel{\overset{\cdots}{—}}\mathrm{CH_2}}}\ \mathrm{Cl^-}.$$

2. The acceleration of ionization by $+E$ substituents in C is best illustrated by the Beckmann rearrangement of oxime esters where the rate increases with $+E$ activity of the acyl and the unsubstituted oximes do not react (p. 219).

3. The effect of $+I$ and $-I$ substituents in B is shown well by the relative rates of $-S_1$ solvolysis of some *tert*-alkyl chlorides.†

$CH_3\cdot CMe_2Cl$	0·854
$MeCH_2\cdot CMe_2Cl$	1·50
$Me_3C\cdot CMe_2Cl$	11·7
$ClCH_2\cdot CMe_2Cl$	0·0002

Methyl is of course a $-I$ substituent, chlorine $+I$.

4. Since methyl is both a $-I$ and a $-E$ substituent, the rate of $-S_1$ reaction increases in the series

$$CH_3I < MeCH_2I < Me_2CHI < Me_3CI.$$

2. $-S_2$ *replacements*

Since C separates as C^- in a $-S_2$ replacement, the effect of substituents in C will be the same as in $-S_1$ replacements; $+I$ or $+E$ substituents will increase, $-I$ decrease, the rate of reaction.

The action of substituents in B is much more difficult to predict. It now appears that three effects must be distinguished.

(*a*) Negative substituents in B will make the B—C bond polar, $\overset{\delta+}{B}—\overset{\delta-}{C}$, and so confer a partial negative charge on C. Hence they will decrease B's hold on the B—C bond electrons and so facilitate ionization of C, either by the $-S_1$ or by the S_2 mechanism. In this case a $-E$ substituent (X) in B apparently acts by a partial electromeric transfer which we may represent in the three systems of notation as

$$\mathrm{X}\overset{\curvearrowright}{—}\mathrm{B}\overset{\curvearrowright}{—}\mathrm{C};\quad \overset{\delta+}{\mathrm{X}}\mathrel{\overset{\cdots}{—}}\mathrm{B}\cdots\overset{\delta-}{\mathrm{C}};\quad \mathrm{X—B—C} \longleftrightarrow \overset{+}{\mathrm{X}}\mathrm{=B}\ \mathrm{C^-}.$$

(*b*) On the other hand, $-I$ substituents in B will give B a partial negative charge. This will increase the energy of approach of a charged reagent A^-, and it will also increase the bond-lengths and decrease the bond-energies A—B and B—C in the transition state of a $-S_2$ replacement, for a negative charge will increase the radius of B. Thus according to (*a*), a $-I$ substituent in B should facilitate $-S_2$ replacement, but according to (*b*) it should retard it. Naturally $+I$ substituents will have the opposite effect. At present it is impossible to predict which effect of a substituent will predominate, but it is found in practice that (*b*) is the more important for inductive substituents and (*a*) the more important for powerful $-E$ substituents. $+E$ substituents accelerate reaction greatly by a special kind of conjugation which stabilizes the transition state (p. 73).

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† For references see Hughes, *Trans. Faraday Soc.* **1941, 37, 624, 626.**

(*c*) The situation is still further complicated by steric hindrance effects. In the series of halides CH_3I, $MeCH_2I$, Me_2CHI, Me_3CI, it is found from a consideration of models† that an attacking anion cannot reach its transition state distance without approaching within less than the van der Waals distance of the α-methyls; that is, the $-S_2$ reaction of methyl iodide with anions will be unhindered, but in the reactions of the other halides additional energy is required to force an attacking anion up to its transition state distance from the central carbon. The calculated energy differences in the above series of halides are comparable to the observed differences in activation energy for their $-S_2$ replacements, and are undoubtedly responsible at least to a large extent for the decrease in $-S_2$ reactivity along the series $MeI > EtI > Pr_{\beta}I > Bu_{\gamma}I$. Fortunately this effect is the same direction as that predicted from (*b*) for the increasing $-I$ activity along the series, so the confusion is less than it might have been.

Steric hindrance is particularly marked in the case of neopentyl halides and analogous β-substituted halides where it leads to an enormous decrease in the rate of $-S_2$ replacement. These reactions will be discussed presently in more detail.

EXAMPLES

The following examples are chosen to illustrate the electronic effect of substituents, the compounds being such that steric factors are constant throughout.

1. That $+I$ substituents increase the rate of replacement is shown by the relative rates‡ of reaction of some bromopropanes with sodium methoxide in methanol.

	Obs.	*Calc.*	*Ratio*
$CH_3 \cdot CH_2 \cdot CH_2Br$	5	(5)	..
$CH_3 \cdot CHBr \cdot CH_3$	1	(1)	..
$Br \cdot CH_2 \cdot CH_2 \cdot CH_2Br$	12	10	1·2
$CH_3 \cdot CHBr \cdot CH_2Br$	33	6	5·5
$Br \cdot CH_2 \cdot CHBr \cdot CH_2Br$	2,450	11	223

The rates calculated on statistical grounds, assuming no effect of substitution, are also given.

The effect is also shown by the relative rates of $-S_2$ replacement of *p*-substituted phenylethyl chlorides with iodide ions,§ the $+I$ effect of the substituent being relayed through the benzene ring. (The substituents are listed in order of decreasing $+I$ activity.)

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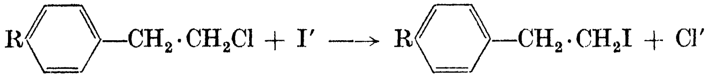
† Evans, *Mem. Proc. Manchester Lit. Phil. Soc.* 1946, **87**; Dostrovsky, Hughes, and Ingold, *J.C.S.* 1946, 173.

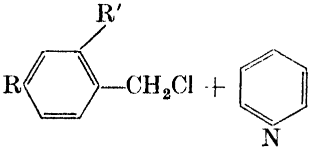
‡ Tronov and Gorsevic, *J. Russ. Phys. Chem. Soc.* 1927, **59**, 727.

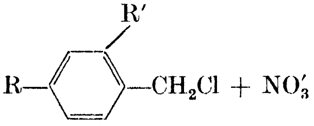
§ Baddeley and Bennett, *J.C.S.* 1935, 1819.



R	Relative rate.
NO_2	3·76
F	1·55
Cl	1·65
Br	1·63
I	1·40
OMe	1·04
H	0·735

2. That $-E$ substituents may increase the rate of $-S_2$ replacement is shown by the relative rates of the Menschutkin reaction[†] of *p*-substituted benzyl chlorides with pyridine. Here the $-E$ effect of the substituent is relayed through the ring (cf. p. 172). The phenyl group itself is a $-E$ substituent, and it is interesting that progressive introduction of positive groups (nitro) first decreases and then increases the rate of reaction; in 2:4-dinitrobenzyl chloride the $-E$ effect of the ring is suppressed, but the $+I$ effect of the substituents then leads to increased reaction rate as in the examples given above. The same effect is shown more clearly in the analogous reactions of benzyl chlorides with nitrate anion; here the inductive effect of the substituents is more important since the reagent is charged and its ease of approach is altered by charges on the side-chain carbon (cf. p. 70).





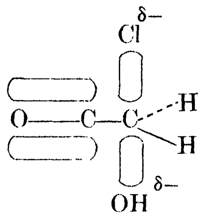
R	R′	*Relative rate*	R	R′	*Relative rate*
NO_2	NO_2	2·29	NO_2	NO_2	33
NO_2	H	1·12	NO_2	H	8·2
H		1·22	H		4·3
Cl		1·27	Bu_γ		6·8
Bu_γ		1·65	Et		7·1
Me		2·02	Me		8·8
Me	Me	6·29			

It is interesting that in these reactions the effect of alkyl groups falls in the series $Me > Et > Pr_\beta > Bu_\gamma$; in this case presumably the $-E$ (hyperconjugation) effect of alkyl is important, in agreement with Hammett's generalization (p. 173).

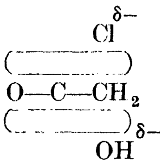
[†] Data quoted from Baker, *Trans. Faraday Soc.* 1941, **37**, 632.

$+E$ substituents

The effect of a $+E$ substituent in B can, however, be predicted unequivocally; it increases the rate of $-S_2$ replacement enormously. For it can conjugate with the partial AB and BC bonds in the transition state. This is most clearly illustrated by an example. The hydrolysis of α-chloroketones proceeds with great ease by the $-S_2$ mechanism. The transition state has the configuration (drawing the relevant electron orbitals diagrammatically)



and the C—O π-orbitals can overlap and conjugate with the C—OH and C—Cl orbitals:



Allyl and benzyl halides likewise undergo $-S_2$ reaction very readily, since both vinyl and phenyl can function as $+E$ substituents.

Structural factors and the choice of mechanism

The rate of an S_1 replacement is independent of the concentration and nature of the anionoid reagent A^-; that of an S_2 replacement increases with the concentration and reactivity of A^-. Therefore an increase in the concentration or reactivity of A^- will encourage the replacement to take place by the S_2 mechanism in preference to S_1, and conversely. In the reaction

$$A^- + Me—\overset{+}{S}Me_2 \rightarrow A—Me + SMe_2$$

the strongly anionoid reagents HO^- and PhO^- react by the S_2 mechanism predominantly, while the reactions with the weakly anionoid reagents CO_3^{--}, Br^-, and Cl^- are essentially unimolecular[†] (S_1).

Secondly, substituents in B affect the S_1 and S_2 rates in opposite ways. Thus $+I$ groups accelerate S_2, retard S_1, while $-I$ groups retard S_2, accelerate S_1. Also $+E$ substituents accelerate S_2 but affect S_1 little, while $-E$ substituents accelerate S_1 but affect S_2 little. Therefore substituents in B will favour one of the two mechanisms at the expense of the other. The alkyl halides afford a classic illustration. Methyl halides replace exclusively by the S_2 mechanism with alkali in aqueous alcohol.

[†] Gleave, Hughes, and Ingold, *J.C.S.* 1933, 1571; 1935, 236.

Introduction of a —I methyl substituent reduces† the rate of reaction, the hydrolysis of ethyl halides being also bimolecular under these conditions. In *iso*-propyl halides the second —I methyl still further reduces the S_2 rate, but the two methyls together accelerate the S_1 reaction so greatly that the S_1 and S_2 replacement rates are comparable. Finally, in *tert*-butyl halides the three methyl groups increase the S_1 rate so much that the (S_1) hydrolysis takes place more rapidly than the (S_2) hydrolysis of methyl halides under the same conditions.‡ Moreover, if the —I effect of one methyl is reversed by substitution with chlorine, as in β-chloro*tert*butyl chloride, $Cl \leftarrow CH_2 \leftarrow CMe_2—Cl$, the S_1 rate falls enormously.§

The effect of E-substituents is even more striking. Thus chloroacetone replaces extremely rapidly with anions|| by the S_2 mechanism, acetyl being a powerful +E substituent, while the rapid replacements of halogen in α-chloroethers and α-dichlorides are unimolecular, alkoxyl and chlorine being —E substituents. In benzyl and allyl halides the phenyl or vinyl substituents have both +E and —E activity; here both S_1 and S_2 mechanisms are facilitated. These halides replace very rapidly and the choice of mechanism depends on the concentration and activity of the anionoid reagent, and on other factors to be discussed later.

Solvent effects

The solvent has an effect on the rate of all replacements, S_1 or S_2, since the charges and charge distributions generally differ in the initial and transition state. Now the energy of solvation of an electrically charged centre in a solvent depends on the magnitude of the charge and the total polarity-cum-polarizability of the solvent molecules. The greater the charge or the greater the polarity-polarizability, the greater the solvation energy. The polarity-polarizability of a solvent varies roughly with its dielectric constant, and so we may correlate the solvation energy with the dielectric constant of the solvent, though it must be remembered that many solvents of high dielectric constant have low solvation energies for ions (e.g. anhydrous HCN, which has the highest known dielectric constant of any liquid but is a very poor solvent for salts).

If the total charge on the reactants in a replacement reaction is less than that of the transition state, the latter will have the higher solvation energy; and this energy will be greater, the greater the dielectric constant of the solvent. The reaction will therefore have a lower activation energy, that is, it will be faster, the higher the dielectric constant of the solvent. This case is well illustrated by the Menschutkin reaction of amines with alkyl halides, e.g.

$$\underset{\text{(uncharged)}}{R_3N\ Me—I} \rightarrow \underset{\text{(charged)}}{R_3\overset{\delta+}{N}\cdots Me\cdots\overset{\delta-}{I}} \rightarrow R_3\overset{+}{N}Me\ I^-.$$

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† Even if the effect of the methyl substituents is mainly steric (p. 71) the general argument still applies.

‡ Hughes, Ingold, and Shapiro, *J.C.S.* 1936, 225; 1937, 1177.

§ Hughes, ibid. 1935, 225; Brown, Kharasch, and Chao, *J.A.C.S.* 1940, **62**, 3435.

|| Conant, Kirner, and Hussey, ibid. 1925, **47**, 488.

This reaction is faster in polar solvents, and in a wide range of solvents the rate is very roughly proportional to the dielectric constant.† The same considerations apply to all S_1 replacements of the type

$$\underset{\text{neutral}}{B{-}C} \rightarrow \underset{\text{charged}}{\overset{\delta+}{B}\cdots\overset{\delta-}{C}} \rightarrow B^+\ C^-$$

for example, the solvolysis of *tert*-butyl halides.‡

Conversely, in an S_2 reaction of the type

$$A^-\quad B{-}C^+ \rightarrow \overset{\delta-}{A}\cdots B\cdots\overset{\delta+}{C} \rightarrow A{-}B\quad C,$$

for example, the decomposition of sulphonium ions by alkali,

$$H\overset{-}{O}\ Me\quad \overset{+}{S}Me_2 \rightarrow H\overset{\delta-}{O}\cdots Me\cdots\overset{\delta+}{S}Me_2 \rightarrow HOMe\ SMe_2$$

the transition state is less charged than the initial state; increase in dielectric constant of the solvent will then stabilize the initial state more than the transition state and so increase the activation energy and retard the reaction.§

A third case is provided by S_2 reactions where the total charges are the same in the initial and transition states, but while in the former the charge is localized on A or C, in the transition state it is shared between A and C:

$$A^- + B{-}C \rightarrow \overset{\delta-}{A}\cdots B\cdots\overset{\delta-}{C}$$

$$A + B{-}C^+ \rightarrow \overset{\delta+}{A}\cdots B\cdots\overset{\delta+}{C}.$$

A similar type is the S_1 reaction of 'onium ions.

$$B{-}C^+ \rightarrow \overset{\delta+}{B}\cdots\overset{\delta+}{C} \rightarrow B^+\ C.$$

Now the energy of solvation of a charge does not depend only on its magnitude; the total solvation energy of two separate small charges is less than the solvation energy of a single charge twice as great. In the transition state of these reactions the initial charge is effectively split into two separate halves; therefore the solvation energy of the transition state is less than that of the initial state. Since the solvation energy varies also with the dielectric constant of the solvent, the difference in energy between the initial and transition states, that is, the activation energy of the reaction, will likewise increase with solvent dielectric constant. Therefore the reaction should proceed more slowly, the higher the dielectric constant of the solvent. Naturally this effect is smaller than the gross effect of charge variation, but nevertheless reactions of this type do occur less readily in solvents of high polarity; for example, the reaction‖

$$Et_3S^+ \rightarrow Et_2S + Et^+ \rightarrow Et_2S + EtX.$$

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† Norris and Prentiss, ibid. 1928, **50**, 3042.

‡ Hughes, *J.C.S.* 1935, 255.

§ Gleave, Hughes, and Ingold, ibid., p. 236.

‖ Hughes and Ingold, ibid., p. 244.

In most reactions the S_1 and S_2 transition states differ in charge distribution. An increase in dielectric constant of the solvent will affect the transition states differently, and so alter the relative rates of the two reactions. A change of solvent may then alter the order of the reaction.

For instance, the hydrolysis of alkyl iodides proceeds by the two mechanisms

$$S_1\text{:}\quad R\text{—}I \rightarrow \overset{\delta+}{R}\cdots\overset{\delta-}{I} \rightarrow R^+\ I^-,$$

$$S_2\text{:}\quad HO^-\ R\text{—}I \rightarrow \overset{\delta-}{HO}\cdots R\cdots\overset{\delta-}{I} \rightarrow HO\text{—}R\ I^-.$$

According to our general principles, an increase in dielectric constant will accelerate the S_1 reaction greatly but will retard the S_2 reaction though to a smaller extent. In the series of halides MeI, EtI, $Pr_{\beta}I$, $Bu_{\gamma}I$ the rate of the S_1 mechanism rises, that of S_2 falls, along the series, as we have already seen. In aqueous acetone, the first three reactions are predominantly bimolecular and the rates fall along the series, but *tert*-butyl iodide hydrolyses vary rapidly by the S_1 mechanism. In aqueous formic acid, however, a solvent with a much higher dielectric constant than aqueous acetone, all the reactions are apparently unimolecular (except possibly that of methyl iodide), and the rates therefore increase steadily along the series,† $MeI < EtI < Pr_{\beta}I < Bu_{\gamma}I$.

Neopentyl and siliconeopentyl halides

An amusing confirmation of the general theory of substitutions was given recently by Dostrovsky and Hughes.‡ Whitmore and his collaborators§ had found that neopentyl halides, $Me_3C\cdot CH_2X$, are extraordinarily inert and undergo normal replacements with extreme difficulty. Moreover, a molecular rearrangement often accompanies such replacements, the products being *tert*-amyl derivatives (p. 208). Dostrovsky and Hughes have found that the reaction of neopentyl bromide with sodium ethoxide in dry alcohol, though abnormally slow, is bimolecular and gives a 'normal' product, ethyl neopentyl ether. Both the activation energy (*E*) and frequency factor (*F*) are abnormal, the former being higher, the latter lower, than those of normal S_2 replacements of primary alkyl bromides under the same conditions, as the following table shows:

	MeBr	EtBr	*iso*-BuBr	$Me_3C\cdot CH_2Br$
E . .	20·0	21·0	22·8	26·2 Cals.
F . .	7×10^{11}	2×10^{11}	9×10^{10}	2×10^{9}

The transition state is evidently restrained in some way, since the frequency factor is small and also its energy of formation is abnormally high.

The solvolytic reaction of neopentyl bromide in aqueous alcohol is, however, unimolecular, and gives the 'abnormal' product, *tert*-amyl alcohol. Moreover, the S_1 solvolysis has approximately the rate to be expected of such a reaction in a primary alkyl halide, so it seems likely that whatever the factors may be that hinder the S_2 reaction, they are not operative in the S_1 solvolysis.

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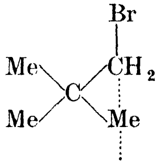
† Bateman, Cooper, Hughes, and Ingold, *J.C.S.* 1940, 925, 945.

‡ *J.C.S.* 1946, 157, 161, 164, 166, 169, 171, 173.

§ Whitmore and Fleming, *J.A.C.S.* 1933, 55, 4161; Whitmore, Popkin, Bernstein, and Wilkins, ibid. 1941, **63**, 124.

The only reasonable explanation seems to be that the methyl groups prevent the transition state for S_2 substitution from adopting its preferred linear configuration. Examination of models shows that it is impossible for the replacing group to approach along the line of the C—Br bond:



Not only is its path of approach circumscribed so that the entropy of formation of the transition state is low and the frequency factor consequently small, but also the reaction has to proceed through energetically unfavourable intermediate states and so its activation energy is high. The whole effect confirms the correctness of the Heitler–London mechanism for such reactions and, moreover, emphasizes the importance of covalency in determining the configuration of the transition state.

Whitmore and his collaborators have shown that all reactions in which the neopentyl cation is formed as an intermediate invariably give *tert*-amyl derivatives. For example, metal halides rearrange neopentyl halides while neopentylamine gives *tert*-amyl alcohol with nitrous acid (cf. p. 210). The apparently normal rate of the S_1 solvolysis of neopentyl bromide, and the formation of *tert*-amyl alcohol, therefore strongly support the ionization mechanism of the reaction, since the ionization would not be subject to steric hindrance and the intermediate neopentyl cation would be expected to rearrange.

These conclusions are supported by two further lines of evidence. Firstly, Whitmore and Sommer† have shown that siliconeopentyl chloride shows none of the abnormalities of neopentyl halides, reacting readily with anionoid reagents to give normal products: e.g.

$$Me_3Si—CH_2Cl + \bar{O}H \rightarrow Me_3Si—CH_2OH + Cl^-.$$

This result is readily intelligible if the unreactivity of neopentyl halides is due to steric hindrance since silicon has a much larger covalent radius than carbon and in siliconeopentyl chloride no hindrance would be expected. Secondly, Dostrovsky and Hughes have pointed out that the unreactivity of pentaerythritol tetrabromide, $C(CH_2Br)_4$, and of β:β-dimethyltrimethylene dibromide, $BrCH_2·CMe_2·CH_2Br$, can be explained in similar terms, and so too can the reactions of α-bromoglutaric acids with strong alkali. Acids with not more than one alkyl substituent in the β-position give α-hydroxyglutaric acids, but in β:β-dialkyl derivatives the normal hydrolysis is hindered and an alternative reaction gives a cyclopropane derivative.

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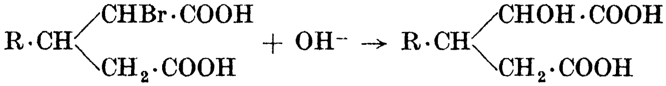
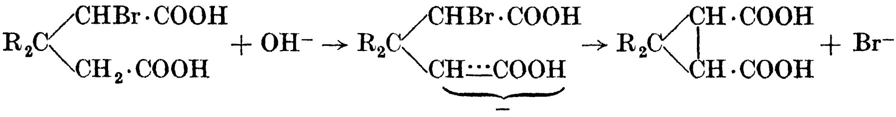
† *J.A.C.S.* 1946, **68**, 481. The S_1 ionization of siliconeopentyl chloride catalysed by $AlCl_3$ does, however, lead to rearrangement; see p. 209.



$$\mathrm{R{\cdot}CH}\left\langle\begin{array}{l}\mathrm{CHBr{\cdot}COOH}\\ \mathrm{CH_2{\cdot}COOH}\end{array}\right. + \mathrm{OH^-} \rightarrow \mathrm{R{\cdot}CH}\left\langle\begin{array}{l}\mathrm{CHOH{\cdot}COOH}\\ \mathrm{CH_2{\cdot}COOH}\end{array}\right.$$

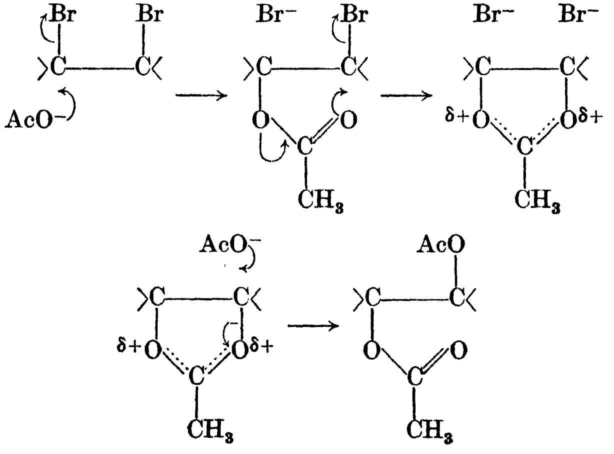


$$\mathrm{R_2C}\left\langle\begin{array}{l}\mathrm{CHBr{\cdot}COOH}\\ \mathrm{CH_2{\cdot}COOH}\end{array}\right. + \mathrm{OH^-} \rightarrow \mathrm{R_2C}\left\langle\begin{array}{l}\mathrm{CHBr{\cdot}COOH}\\ \underbrace{\mathrm{CH{\cdots}COOH}}_{-}\end{array}\right. \rightarrow \mathrm{R_2C}\left\langle\begin{array}{l}\mathrm{CH{\cdot}COOH}\\ |\\ \mathrm{CH{\cdot}COOH}\end{array}\right. + \mathrm{Br^-}$$

The general theory explains these facts well.

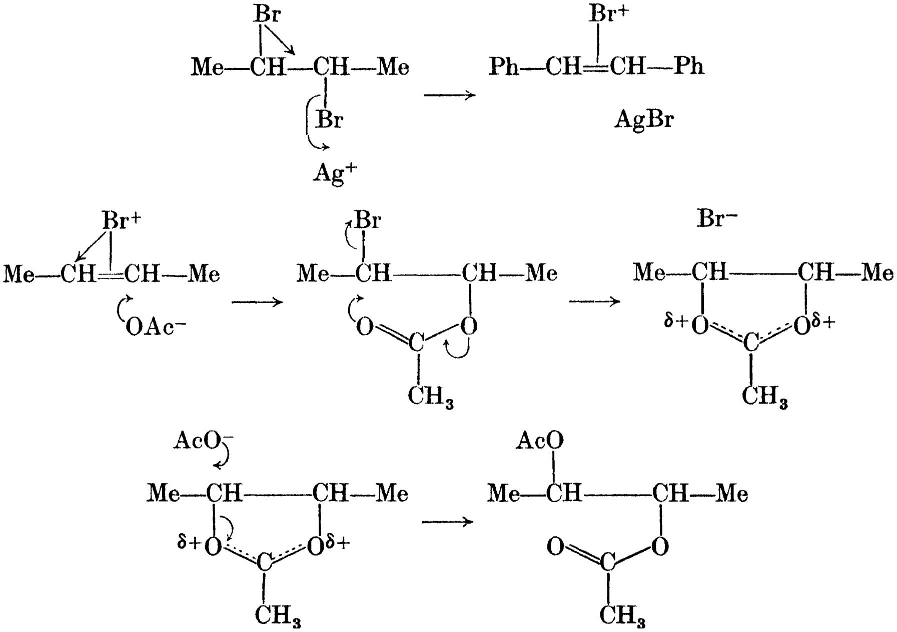
Complex replacements

Sometimes the replacement reaction gives a product with the same configuration as the starting material, a result apparently in conflict with the general theory. It now seems probable that each such reaction involves two steps, each step being a normal S_2 replacement. Since each replacement leads to inversion, the product is formed by double inversion, that is, with retention of configuration. Thus in the reaction of 1:2-dibromides with sodium acetate to form glycol diacetates, one bromine replaces with retention of configuration, one with inversion. Apparently one bromine first replaces with inversion; the resulting bromoethyl acetate then undergoes an internal S_2 replacement of bromine to form a cyclic intermediate and this with the second acetate ion undergoes a further S_2 replacement to form the diacetate.

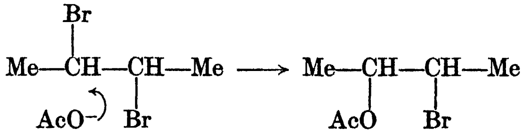


Therefore the first bromine replaces with single inversion, the second with double inversion or retention of configuration.

The reactions of the 2:3-dibromobutanes with silver acetate in acetic acid are interesting.† Under absolutely anhydrous conditions, the product from *meso*-dibromide is pure *meso*-diacetate; but in presence of small amounts of water equally pure *dl*-diacetate is formed. Since the action of the ion Ag^+ on halides is essentially cationoid (p. 81), it is most unlikely that the conversion of *meso*-dibromide to *meso*-diacetate takes place by inversion at both carbons. A much more reasonable explanation seems to be that both replacements involve double inversion and cyclic intermediates; therefore both take place with retention of configuration. The first intermediate was originally formulated with a 3-membered ring but it is more probably a π-complex (p. 18).



Solutions of silver acetate in anhydrous solvents probably do not contain enough acetate ion for a direct bimolecular attack; therefore in absence of water cationoid removal of chlorine is the first step. In presence of water more acetate ions are present and the first step is a simple anionoid replacement with inversion. The subsequent reactions, leading to substitution of the second bromine by double inversion, are the same as before, but this time the first replacement takes place in one stage only with inversion.



Another example is the conversion of 2:3-butylene bromohydrin to the dibromide with retention of configuration† on boiling with hydrobromic acid. The mechanism is presumably

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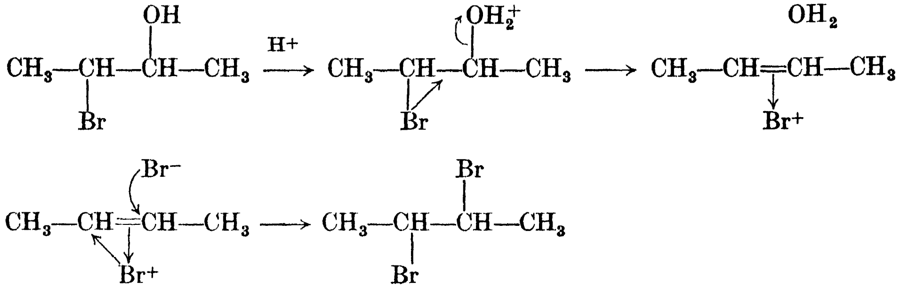
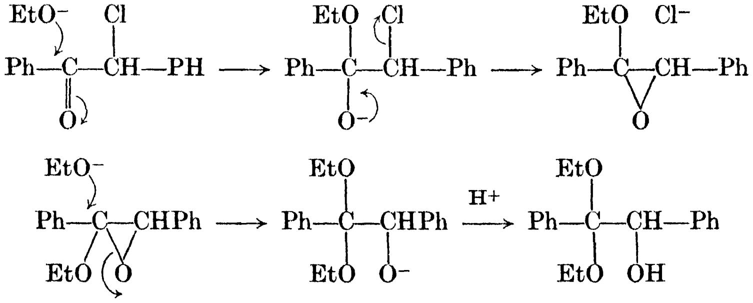
† Winstein et al., *J.A.C.S.* 1942, **64**, 2780, 2787, 2791, 2792, 2796.



where again the intermediate is formulated as a π-complex rather than with a 3-membered ring formed by normal valencies. Similar again is the reaction of chlorodesoxybenzoin with sodium ethoxide to form benzoin acetal;‡ benzoin does not form the acetal under these conditions and the mechanism is probably



The first step is a carbonyl addition, and two S_2 replacements follow.

An illuminating example of double inversion has been discovered by Kenyon, Phillips, and Taylor.§ The hydrolysis of *l*-α-phenylethyl toluenesulphonate with potassium carbonate in alcohol gives *d*-α-phenylethyl alcohol, presumably by a normal S_2 replacement; but in presence of a large excess of lithium chloride the *l*-alcohol is formed. This can only be explained if the toluenesulphonate first reacts with chloride ion to give *d*-α-phenylethyl chloride, and this then hydrolyses to the *l*-alcohol, both reactions being normal S_2 replacements and taking place with inversion.

$$l[\mathrm{Ph{\cdot}CHMe{\cdot}O{\cdot}SO_2C_7H_7}] + \mathrm{Cl^-} \rightarrow d[\mathrm{Ph{\cdot}CHMe{\cdot}Cl}]$$

$$d[\mathrm{Ph{\cdot}CHMe{\cdot}Cl}] + \mathrm{OH^-} \rightarrow l[\mathrm{Ph{\cdot}CHMe{\cdot}OH}]$$

The process is exactly analogous to the iodide-catalysed reactions of alkyl chloride and bromide (p. 68).

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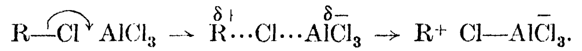
† Winstein and Lucas, *J.A.C.S.* 1939, **61**, 1576.
‡ Ward, *J.C.S.* 1929, 1541.
§ *J.C.S.* 1933, 173.

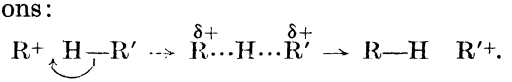
Cationoid replacements

Reactions of the type $A^+ + BC \rightarrow AB + C^+$, when A^+ is cationoid reagent, have been little investigated, but they undoubtedly conform to the same general principles as do their anionoid counterparts. Cationoid replacements on carbon, that is, reactions where the central atom of B is carbon, do not seem to have been reported, but replacements on hydrogen or halogen are known. All are probably of the S_2 type and so they will be facilitated by increase in cationoid reactivity of A^+ or in ease of ionization of C as a positive ion. The simplest reactions of this type are the conversions of alkyl halides to cations by aluminium chloride, integral steps in the Friedel-Craft alkylations of aromatic hydrocarbons (p. 178):



$$R{-}Cl\ AlCl_3 \rightarrow \overset{\delta+}{R}\cdots Cl\cdots \overset{\delta-}{AlCl_3} \rightarrow R^+\ Cl{-}\overset{-}{Al}Cl_3.$$

The alkyl cations so formed can effect an analogous replacement of alkyl from hydrocarbons:



$$R^+\ H{-}R' \rightarrow \overset{\delta+}{R}\cdots H\cdots \overset{\delta+}{R'} \rightarrow R{-}H\quad R'^+.$$

This reaction should occur more readily, the more the transition state is stabilized by substituents. Since negative substituents in R′ should conjugate with it in the transition state, they should reduce the activation energy of the reaction and increase its rate. Therefore —I alkyl groups should accelerate the reaction and therefore hydrogen atoms should react the more readily, the more heavily alkylated the carbon to which they are attached. This seems to be the case, and indeed the reactions of tertiary hydrogen atoms are extraordinarily rapid. A mixture of *tert*-butyl chloride and 2-methylbutane when treated with aluminium bromide reacts to give *iso*-butane and *tert*-amyl bromide almost instantaneously. The mechanism is presumably

$$Me_3C{-}Cl + AlBr_3 \rightarrow Me_3C^+ + ClAlBr_3^-$$

$$Me_3C^+ + H{-}CMe_2Et \rightarrow Me_3CH + \overset{+}{C}Me_2Et$$

$$\overset{+}{C}Me_2Et + Cl\overset{-}{Al}Br_3 \rightarrow Me_2EtC{-}Br + AlClBr_2.$$

No doubt an equilibrium is set up, since the reactions must all be reversible, but *tert*-amyl halide is favoured. (In the halides the C–hal bond is polar and the carbon therefore carries a positive charge. While this structure is stabilized by the —I effect of three alkyls in both *tert*-butyl and *tert*-amyl halides, the latter are more stabilized since the —I effect of ethyl is greater than that of methyl.)

The ionization of alkyl halides can also be induced by cationoid metallic ions, particularly silver and mercurous ions. It has long been known that silver or mercurous salts catalyse the solvolysis of alkyl halides, and the mechanism seems undoubtedly to be

$$R{-}X + Ag^+ \rightarrow R^+\ AgX$$

$$R^+ + \text{solvent} \rightarrow \text{product}.$$

Silver and mercurous ions are known to have an extraordinary affinity for halogen, and this mechanism is also supported by direct evidence. Firstly, as Hammett has remarked, in the solvolysis of benzyl chloride catalysed by mercurous salts a yellow colour develops during the reaction and fades as it approaches completion. This might be expected if benzyl cations are intermediates since there are theoretical reasons for supposing that the benzyl cation is intensely coloured. Secondly, the silver-catalysed solvolysis of neopentyl chloride proceeds at a normal rate to give rearranged products;† here again it seems extremely likely that the neopentyl cation is first formed.

Reduction and oxidation as replacement reactions

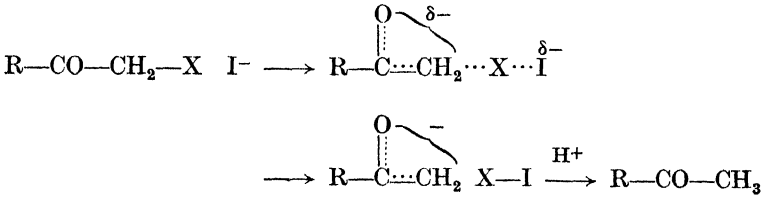
In the most general terms, reduction consists in the giving of electrons to a compound, oxidation in the removal of electrons. In many cases such reactions are brought about by the donation or removal of electron-rich groups and may then be regarded as replacements of special type. Thus the reactions of a hydrocarbon RH with an alkyl halide in presence of aluminium chloride to give a halogen derivative may be regarded as an oxidation, the essential step being a cationoid removal of a hydrogen atom with a pair of electrons intact, i.e. of an H^- ion.

$$RCl + AlCl_3 \rightarrow R^+ + AlCl_4^-$$

$$R^+ + \overset{\curvearrowleft}{H}—R' \rightarrow RH + R'^+$$

$$R'^+ + AlCl_4^- \rightarrow R'Cl + AlCl_3.$$

Again, the reduction of α-haloketones by iodide ion is really an anionoid replacement on halogen,



$$R—CO—CH_2—X \quad I^- \longrightarrow R—\overset{\overset{\delta-}{O}}{\overset{\vdots}{C}}\cdots CH_2\cdots X\cdots \overset{\delta-}{I}$$

$$\longrightarrow R—\overset{\overset{-}{O}}{\overset{\vdots}{C}}\cdots CH_2 \quad X—I \xrightarrow{H^+} R—CO—CH_3$$

and is made possible by mesomeric stabilization of the transition state by the +E carbonyl group. Other reductions and oxidations of similar type are known, especially ones involving radical rather than ionic replacements (see Chapter XIII). An amusing combination of the two reactions cited above has been reported;‡ on heating neopentyl iodide with sodium ethoxide in alcohol, reduction takes place, normal replacement being hindered (p. 76). The reaction effectively involves transfer of a hydrogen atom with its pair of electrons intact.

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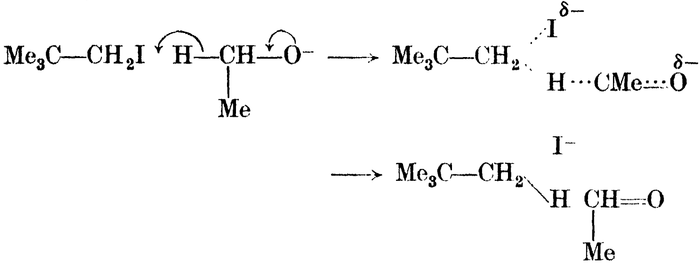
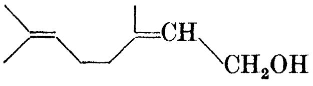
† Hughes and Dostrovsky, *J.C.S.* 1946, 169.

‡ Whitmore, Wittle, and Popkin, *J.A.C.S.* 1939, 61, 1586.

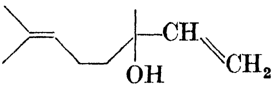


Anionotropy

A number of anionoid replacement reactions of allyl derivatives are known where rearrangement accompanies replacement. The classical example of this reaction is the interconversion of geraniol (III) and linalaol (IV) by anionoid replacements of their derivatives. Thus hydrolysis of the acetate of either compound gives a mixture of the two isomeric alcohols.



(III)



(IV)

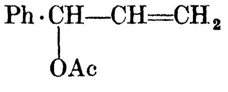
Farnesol and nerolidol are likewise interconvertible, as are the four isomers codeine, *pseudo*-codeine, *iso*-codeine, and *allopseudo*-codeine. These rearrangements were somewhat puzzling to the older organic chemists since a given reaction might or might not lead to rearrangement under apparently equivalent conditions. Thus cinnamyl chloride (V) with sodium acetate in acetic anhydride gives only cinnamyl acetate (VI), while in acetic acid alone, a mixture of cinnamyl and α-phenylallyl (VII) acetates is obtained.†

$Ph\cdot CH{=}CH\cdot CH_2Cl$

(V)

$Ph\cdot CH{=}CH\cdot CH_2\cdot OAc$

(VI)



$Ph\cdot \underset{OAc}{CH}{-}CH{=}CH_2$

(VII)

Burton and Ingold‡ first suggested the mechanism for these rearrangements which is now generally accepted. In an S_1 replacement of an allyl derivative, the intermediate is an allyl cation which is mesomeric and completely symmetrical. In the subsequent reaction of this cation with the anionoid reagent, two products can be formed by reaction with either end of the allylic system; thus the solvolysis of crotyl chloride (VIII) in alcohol gives a mixture of crotyl (IX) and α-methylallyl (X) ethyl ethers by the following mechanism:

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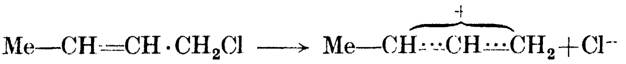
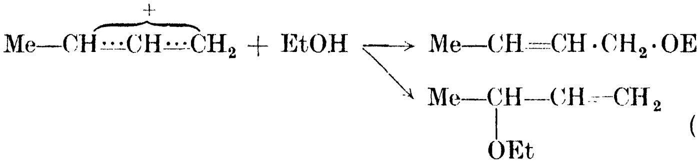
† Meisenheimer and Beutter, *Annalen*, 1934, **508**, 58.

‡ *J.C.S.* 1928, 904, 1650; 1929, 455.

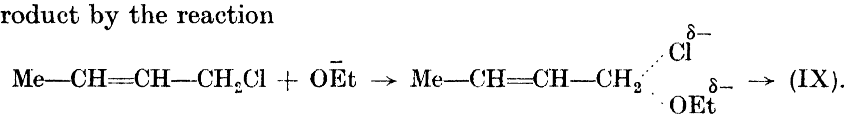


$$\underset{\text{(VIII)}}{\mathrm{Me{-}CH{=}CH\cdot CH_2Cl}} \longrightarrow \underset{\text{(XI)}}{\mathrm{Me{-}\overbrace{CH{\cdots}CH{\cdots}CH_2}^{+}}} + \mathrm{Cl^-}$$



$$\mathrm{Me{-}\overbrace{CH{\cdots}CH{\cdots}CH_2}^{+} + EtOH}\ \begin{array}{l} \longrightarrow \mathrm{Me{-}CH{=}CH\cdot CH_2\cdot OEt} \quad \text{(IX)} \\ \searrow \mathrm{Me{-}\underset{\displaystyle OEt}{\underset{|}{CH}}{-}CH{=}CH_2} \quad \text{(X)} \end{array}$$

If this mechanism is correct, the S_2 replacement should give a normal product by the reaction



$$\mathrm{Me{-}CH{=}CH{-}CH_2Cl + \bar{O}Et \rightarrow Me{-}CH{=}CH{-}CH_2}\begin{array}{l}\cdot\,\overset{\delta-}{\mathrm{Cl}}\\ \cdot\,\overset{\delta-}{\mathrm{OEt}}\end{array} \rightarrow \text{(IX)}.$$

These conclusions have been confirmed in detail by Catchpole.† With sodium ethoxide in dry alcohol both crotyl chloride and α-methylallyl chloride give the corresponding ethers without rearrangement by a bimolecular (S_2) reaction. In the absence of ethoxide, however, the S_1 reaction predominates and the products from both chlorides are mixtures of both possible ethers. Furthermore, the proportions of the ethers are now the same in both cases, a result which must mean that both solvolyses proceed through a common intermediate—which can only be the corresponding allyl cation (XI). These results have been confirmed by Young and Andrews,‡ who showed that the S_1 solvolysis of both chlorides in aqueous alcohol gives the same mixture of crotyl and α-methylallyl alcohols. With aqueous alcoholic alkali the order of the reaction with crotyl chloride depended on the alkali concentration (cf. p. 73) being unimolecular at low alkali concentrations and bimolecular at high alkali concentrations. As the S_2 replacement becomes more important, the proportion of crotyl alcohol in the product increases.

Incidentally, the acetolysis of cinnamyl chloride, mentioned above, has also been studied kinetically by Meisenheimer and Beutter (loc. cit.). They found, as the theory requires, that the normal replacement with acetate ion in acetic anhydride is bimolecular, while the solvolysis in acetic acid is largely unimolecular. Only the latter (S_1) reaction leads to rearrangement.

Rearrangements of this general type are called *anionotropic*, since they involve a separation of an anion. In an inert solvent the anion may actually recombine with the allyl cation to regenerate an isomer of the starting material. Thus α-phenylallyl *p*-nitrobenzoate (XII) in acetic anhydride rearranges to cinnamyl nitrobenzoate. If acetate ions are added, a competitive reaction gives cinnamyl acetate.†

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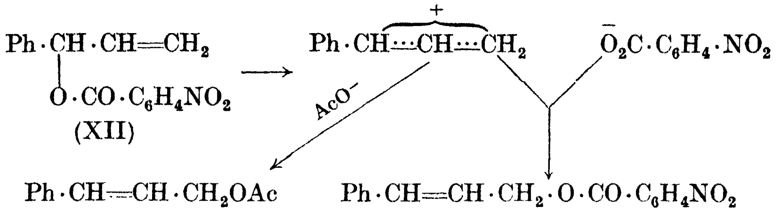
† Quoted by Hughes, *Trans. Faraday Soc.* 1941, **37**, 628.
‡ *J.A.C.S.* 1944, **66**, 421.



Structural effects in anionotropy

For anionotropy to occur, the S_1 mechanism must be possible. This condition is automatically fulfilled in allyl derivatives since the vinyl group is a powerful S_1 activator. Extra negative substituents will further assist S_1 replacement and hence rearrangement. Thus crotyl chloride (VIII) gives the normal product, crotyl alcohol, with strong aqueous alcoholic alkali by the S_2 mechanism, but α-methylallyl chloride still hydrolyses unimolecularly under these conditions to give a mixture of crotyl and α-methylallyl alcohols. In the latter case the S_1 mechanism is favoured because there is an extra negative group (—I methyl) present.

After ionization, the allyl cation can combine with the anionoid reagent in two ways. If the cation is unsymmetrical, one or other product will be favoured. The transition states for the two reactions of an allyl cation $\overset{+}{\overbrace{C^1 \cdots C^2 \cdots C^3}}$ with an anion A^- will be

$$\overset{\delta-}{A}\cdots\overset{\delta+}{C^1}—C^2=C^3 \quad \text{and} \quad C^1=C^2—\overset{\delta+}{C^3}\cdots\overset{\delta-}{A}.$$

The substituents in a substituted allyl cation may conjugate or hyperconjugate with the double bond in the transition complex and so stabilize it. (The substituent will have less effect on the cation itself since in it the substituent is conjugating with a bond of lower order than the 'almost double' bond in the transition state.) A substituent on C^2 will stabilize both transition states equally, but a substituent on a terminal carbon atom will affect one transition state only. In the latter case, then, the reaction should give preferentially the isomer in which the double bond is conjugated with the substituent. Thus α-phenylallyl p-nitrobenzoate gives with acetate ion in acetic anhydride almost pure cinnamyl acetate, while in the mixture of alcohols from the solvolysis of crotyl or α-methylallyl chlorides, crotyl alcohol predominates. In each product the substituent (phenyl or methyl) is conjugated or hyperconjugated with the double bond.

S_2 anionotropy

Hughes‡ has suggested that an alternative form of the S_2 replacement should be possible in allyl compounds, giving a rearranged product. The anionoid reagent should in theory be able to attack the γ-carbon. This mechanism can be represented

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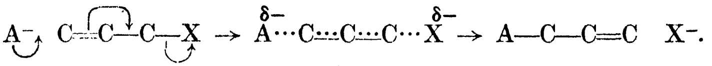
† Burton and Ingold, *J.C.S.* 1928, 904, 1650; 1929, 455.

‡ *Trans. Faraday Soc.* 1938, **34**, 185.

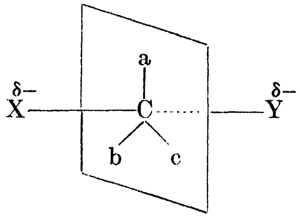


$$A^- \; C{=}C{-}C{-}X \rightarrow \overset{\delta-}{A}\cdots C\,\overset{..}{\cdots}\,C\,\overset{..}{\cdots}\,C\cdots\overset{\delta-}{X} \rightarrow A{-}C{-}C{=}C \quad X^-.$$

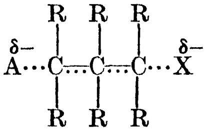
(XIII)

No definite example of this mechanism is known, and there is a very good reason why this should be so. We may give the argument in full since it will be useful later in considering the reactions of carboxylic acids.

In the transition state of a normal anionoid replacement on carbon, the central atom has a trigonal bipyramidal configuration;



evidently one p-orbital is used to form the bonds with X and Y, while the remaining s- and p-orbitals form normal sp_2-hybridized bonds with the other three groups. For stability to be a maximum, X, C, and Y must be collinear, a p-orbital having lobes separated by 180° and therefore bonding most efficiently in those directions. In the transition state (XIII) for the S_2 rearrangement reaction, the terminal groups must similarly be bonded by the lobes of p-orbitals; the other dotted bonds must be formed by the remaining lobes, and by the lobes of a similar p-orbital of the central carbon. The transition state must therefore be linear. Each of the carbon atoms must also contribute a p-orbital towards the allylic π-bonds (represented in the diagram by full lines). Each carbon must therefore form its two remaining bonds from an s-orbital and a p-orbital by sp-hybridization. The sp-hybrid bonds are best formed at an angle of 180°; the whole structure will then be linear and planar, thus:

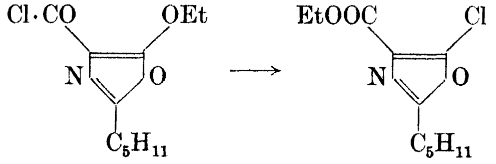


$$\overset{\delta-}{A}\cdots\underset{R}{\overset{R}{C}}\,\overset{..}{\cdots}\,\underset{R}{\overset{R}{C}}\,\overset{..}{\cdots}\,\underset{R}{\overset{R}{C}}\cdots\overset{\delta-}{X}$$

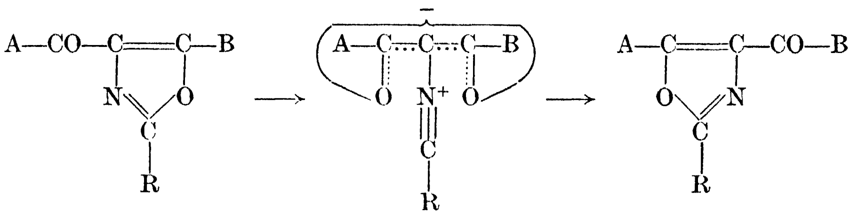
Now in the first place such a structure would undoubtedly be more rigid than a normal S_2 transition state and its entropy would therefore be low. Hence the reaction involving it would have an abnormally low frequency factor. In the second place, the transition state contains two normal bonds less than the initial state, and its energy of formation should therefore be much higher than that of a normal S_2 transition state, where one bond only is broken. Therefore the S_2 rearrangement should have both a high activation energy and a low frequency factor, and it is unlikely that any example of it will be found.

Intramolecular anionotropy

Cornforth and his collaborators† have recently discovered a number of rearrangements in the oxazole series which seem to take place by intramolecular anionotropy. The prototype was the conversion of 2-amyl-5-ethoxyoxazole-4-carboxylic acid chloride (XIV) into ethyl 2-amyl-5-chlorooxazole-4-carboxylate (XV) by heat. The reaction is rather general for oxazole derivatives of the type (XVI), where A, B may be halogen, alkyl, hydrogen, or amino groups. The only reasonable mechanism is the one indicated, the intermediate being an open-chain zwitterion.



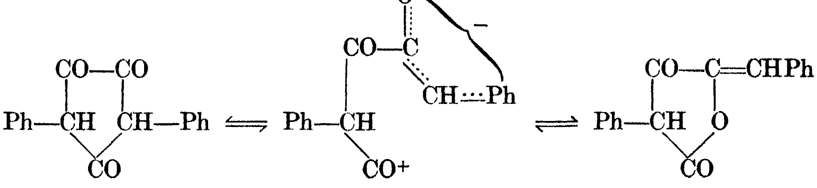
(XIV) (XV)



(XVI)

The reaction is an anionotropic rearrangement in which the ions are held together by the rest of the molecule. It is made possible by the low resonance energy of the oxazole ring (which is lost in the ionization), the mesomeric stabilization of the negative ion, and the stabilization of the positive ion by transference of the charge to nitrogen. A kinetic study of this reaction would be well worth while. If this mechanism is correct it should occur more readily in polar solvents.

A similar reaction has recently been reported by Schönberg and Sina;‡ 1:3-diphenylcyclopentatrione (XVII) is reversibly converted by heat into an isomeric lactone (XVIII). The only reasonable mechanism is the one indicated, again an intramolecular anionotropy.



(XVII) (XVIII)

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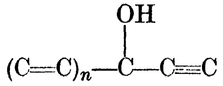
† Private communication from Dr. J. W. Cornforth.

‡ *J.C.S.* 1946, 601.

Here the negative charge is again stabilized by mesomerism while the carbonyl group is known to occur as a cation in the aluminium chloride complexes of acyl halides (p. 179).

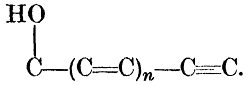
Complex anionotropy

Heilbron, Jones, and their collaborators† have discovered a remarkable rearrangement in the polyene series; alcohols of the type



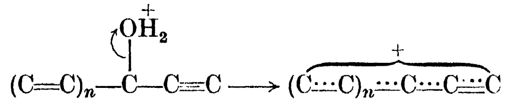
$$(C{=}C)_n{-}\overset{\overset{\displaystyle OH}{|}}{C}{-}C{\equiv}C$$

on treating with acid rearrange to completely conjugated isomers



$$\overset{\overset{\displaystyle HO}{|}}{C}{-}(C{=}C)_n{-}C{\equiv}C.$$

The mechanism is clearly similar to the normal anionotropy of allyl compounds; the alcohol first forms a salt (XIX) which then ionizes to the mesomeric ion (XX). This ion can combine again with hydroxyl ion in a number of ways, but terminal addition is naturally favoured since the transition state for such addition is more highly conjugated than that for any of the other possible reactions.



$$(C{=}C)_n{-}\overset{\overset{\displaystyle \overset{+}{O}H_2}{|}}{C}{-}C{\equiv}C \longrightarrow \overbrace{(C{\cdots}C)_n{\cdots}C{\cdots}C{\equiv}C}^{+}$$

(XIX) (XX)

This mechanism has been supported by various kinetic measurements and certainly no other could account for migrations of hydroxyl from one end to the other of an extensive conjugated chain.

General classification of reactions

The division of replacement reactions into two types, S_1 and S_2, is a special case of a general phenomenon. In all reactions where one or more bonds are broken and others are formed, two general types of mechanism are possible; in one the bond-breaking precedes bond-formation, the reaction occurring in two steps, while in the other both processes are simultaneous (cf. p. 25). Ingold and his collaborators have found a similar dichotomy into 'unimolecular' and 'bimolecular' types in a number of other reactions and have proposed an intricate system of nomenclature for them. It seems very much better to retain the original 'S' notation for reactions in general, since the distinction between unimolecular and bimolecular types is the same for all. Six general reaction-types are then possible, four ionic reactions $\pm S_1$, $\pm S_2$, and two radical reaction types which we may term OS_1 and OS_2.

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† See Johnson, *The Chemistry of the Acetylenic Compounds*, Edward Arnold, 1946.

CHAPTER VI

ACIDS AND BASES. PROTOTROPIC AND ELIMINATION REACTIONS

According to Bronsted's generalized definition of acids and bases, an acid is any substance which can donate protons, a base any substance which can accept them. In this sense all compounds of hydrogen must be acids, while all compounds containing one or more pairs of unshared electrons must be bases. Naturally the ability to donate protons, i.e. the acid strength, varies enormously in different hydrogen compounds, as likewise does the ability to accept protons in bases.

The earlier view of acids was that their acidity depended on their ability to ionize to free protons. We now know, however, that such reactions never occur under normal conditions. When an acid 'dissociates' in solution, it does so only by transferring a proton to a base. Thus in aqueous solutions of acids, water itself acts as a base, forming oxonium ions.

$$HA + H_2O \rightleftharpoons A^- + H_3O^+$$

In completely non-basic solvents, e.g. paraffin hydrocarbons, acids do not dissociate at all unless a base is also added.

The dissociation of an acid gives an anion which can recombine with a proton to regenerate the acid; the anion is therefore a base. Similarly the combination of a base with a proton gives an acid. Such pairs of related acids and bases are called *conjugate*; thus the acetate ion is the conjugate base of acetic acid, while acetic acid is the conjugate acid of the acetate ion.

The reaction of an acid (HA) with a base (B) therefore leads to an equilibrium, and the equilibrium constant

$$K = \frac{[A^-][BH^+]}{[HA][B]}$$

is a measure of the strengths of the acid and base. A quantitative measure of acid strengths is thus provided by the equilibrium constants of their reactions with a standard base. Normally water is taken as standard, the equilibrium constant (dissociation constant) being measured in water as solvent. Since the concentration of the water varies little it is usual to write the dissociation constant as

$$K_A = \frac{[A^-][H_3O^+]}{[HA]}.$$

It is often convenient to give not K_A for the acid but pK_A, where $pK_A = -\log_{10} K_A$. Thus the dissociation constant of an acid with $pK = 3$ is 10^{-3}.

Since water is also a weak acid, reacting with bases according to the equation

$$B + H_2O \rightleftharpoons BH^+ + OH^-,$$

it is possible to measure the strength of bases from their dissociation constants in water (the concentration of water is again assumed to be constant)

$$K_B = \frac{[BH^+][OH^-]}{[B]}.$$

Moreover, since water is both an acid and a base, it can react with itself according to the equation

$$2H_2O \rightleftharpoons H_3O^+ + OH^-.$$

Therefore

$$[H_3O^+][OH^-] = K_W \simeq 10^{-14},$$

where K_W is the 'self-dissociation constant' of water (once again the concentration of water is assumed to be constant).

Now the basic dissociation constant of the conjugate base A^- of the acid HA is given by

$$K_{A^-} = \frac{[HA][OH^-]}{[A^-]},$$

whence it is seen that $K_A K_{A^-} = K_W$.

Hence the stronger an acid, the weaker its conjugate base, and conversely.

Measurements of acid strengths are only possible in water for acids with strengths within a certain range. Acids which are weaker than water itself do not dissociate measurably, while acids stronger than the oxonium ion (H_3O^+) are dissociated too completely. Likewise bases can only be investigated quantitatively in water if their strengths lie between those of water and the hydroxyl ion. The investigation of very weak acids and bases is, however, possible in solvents of sufficiently high basicity or acidity. Thus very weak bases may be examined in acetic, formic, or sulphuric acids, while weak acids may be examined in aniline. Again strong acids may be studied in weakly basic solvents; thus trichloracetic acid is almost completely dissociated in water, but only partly so in alcohol, which is a weaker base than water. In this way the relative strengths of acids and bases can be measured over a wide range. Moreover, the relative strengths of two extremely weak acids HA and HB may be found from the equilibrium between one acid and the conjugate base of the other, in an inert solvent:

$$HA + B^- \rightleftharpoons A^- + HB$$

$$K = \frac{[HA][B^-]}{[A^-][HB]} = \frac{K_{HB}}{K_{HA}}.$$

The relative strengths of acids and bases seem to be roughly the same in different solvents, so these methods enable us to extrapolate our measurements to regions of acidity and basicity not accessible in water, and at the same time to express the results in terms of the original pK scale. Some examples are given below. (It should be added that dissociation constants vary with temperature. The values given in the chapter refer to room temperature, most of them to 25°.)

TABLE 12

Very weak bases†		*Very weak acids*‡	
Base	pK_B	*Acid*	pK_A
p-Nitraniline . .	12·9	Methane . .	50
2:4-Dinitraniline .	18·4	Cumene . .	37
Picramide . .	23·3	Aniline . .	27
Acetophenone .	20·0	Phenylacetylene .	21
Benzoic acid . .	21·3	*t*-Butanol . .	19

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† Hammett et al., *J.A.C.S.* 1932, **54**, 2721; 1934, **56**, 827; 1935, **57**, 2103; 1938, **60**, 885; 1939, **61**, 2785.

‡ Conant and Wheland, ibid. 1932, **54**, 1212; McEwen, ibid. 1936, **58**, 1124.

Relation between structure and the strength of acids

The dissociation constant of an acid may be expressed in terms of the free energy, entropy, and heat of dissociation as

$$K = e^{-\Delta F/RT} = e^{\Delta S/R}e^{-\Delta H/RT}.$$

Therefore the smaller the free energy of dissociation into ions, the larger K and the stronger the acid. We must again assume that the entropy changes are constant so that the value of K depends only on the heat of dissociation. For the reaction

$$\mathrm{HA}+\mathrm{H_2O} = \mathrm{A^-}+\mathrm{H_3O^+}$$

we have

$$\Delta H = E_{\mathrm{HA}}+E_{\mathrm{H_2O}}-E_{\mathrm{A^-}}-E_{\mathrm{H_3O^+}},$$

where the E's are the various heats of formation. Since $E_{\mathrm{H_2O}}$ and $E_{\mathrm{H_3O^+}}$ are the same in all cases, we have

$$\Delta H = \text{constant}-E_{\mathrm{A^-}}+E_{\mathrm{HA}}.$$

An analysis along the same lines as those followed in the previous chapter then leads us to the conclusion that ΔH should be smaller, and the acid stronger,

(1) the smaller the H—A bond-energy;
(2) the greater the electron-affinity of A;
(3) the greater the resonance energy of $\mathrm{A^-}$ compared with that of HA.

1. The effect of the HA bond-energy is relatively unimportant. It probably accounts, however, for the fact that acid strength increases in the series HF < HCl < HBr < HI, although electron-affinity falls in the order F > Cl > Br > I.

2. The effect of electron-affinity is usually very important. Firstly, the relative acid strengths of hydrides depend greatly on the electron-affinity

of the central atom. Thus the electron-affinities of C, N, O, F rise in that order while the approximate *pK*'s of their hydrides are

CH_4	50
NH_3	30
OH_2	14
HF	3·5

Secondly, introduction of I-substituents into such hydrides alters the electron-affinity of the central atom and so the acid strength. This is illustrated in Table 13. According to the general principles, +I substituents should increase, —I decrease, the acid strength.

TABLE 13

(*a*) *Effect of* —I *substituents*

H_2O	14	$HCOOH$	3·7
MeOH†	16	$H_3C\cdot COOH$	4·7
EtOH†	18	$MeCH_2\cdot COOH$	4·9
Bu_γOH†	19	$Me_3C\cdot COOH$	6·0

(*b*) *Effect of* +I *substituents*

Mannitol	13·5	$CH_3\cdot COOH$	4·7	$Me\cdot CO\cdot CH_3$‡	20·0
Sorbitol	13·5	$CH_2Cl\cdot COOH$	2·9	$MeCO\cdot CH_2Cl$‡	16·5
Mannose	12·0	$CHCl_2\cdot COOH$	1·3	$MeCO\cdot CHCl_2$‡	14·9
Glucose	12·3	$CCl_3\cdot COOH$	< 0		
H_2O	14	$CH_2OH\cdot COOH$	3·8		
H_2O_2	11·6	$CH_2CN\cdot COOH$	2·4		
ClOH	6·8				

3. Introduction of +E substituents into a hydride greatly increases the resonance energy of the conjugate base, but increases that of the hydride to a much smaller extent. Such substituents therefore greatly increase the acidity. Examples are given in Table 14.

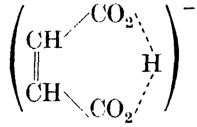
TABLE 14

H_2O	14	CH_4	~ 50
$CH_3CO\cdot OH$	4·7	$MeCO\cdot CH_3$‡	20·0
$O_2N\cdot OH$	< 0	$PhCO\cdot CH_3$‡	19·2
$HSO_3\cdot OH$	< 0	$(MeCO)_2CH_2$‡	9·3
$O_3Cl\cdot OH$	< 0	$(MeCO)_3CH$	5·9
H_2S	7·1	$O_2N\cdot CH_3$	11·0
$CH_3CO\cdot SH$	3·3	$(O_2N)_2CHMe$	5·2
H_3N	~ 25	$(O_2N)_3CH$	< 0
$CH_3CO\cdot NH_2$	14	$PhCH_3$†	37
$NC\cdot NH_2$	7	Ph_2CH_2†	35
$O_2N\cdot NHMe$	6·1	Ph_3CH†	33
$CH_3CO\cdot NH\cdot CN$	3·8		

† See Table 12.

‡ Bell, *Trans. Faraday Soc.* 1943, **39**, 253.

One further interesting effect is shown in acids containing a highly polar group in proximity to the dissociatable hydrogen. A direct electrostatic attraction or repulsion of the nascent proton may increase or decrease the dissociation energy. Thus in dibasic carboxylic acids the second dissociation constant is unusually small; because the carboxylate ion formed by dissociation of one carboxyl attracts the proton formed by dissociation of the other, and it therefore reduces the tendency of the second proton to escape, i.e. lowers the dissociation constant of the other acid group. This effect is seen in all the lower aliphatic acids, but of course it diminishes with increasing separation of the acid groups. A similar effect is seen in maleic acid; here the polar carboxyl groups repel each other strongly, but in the ion formed by half-dissociation they actually attract each other, being linked by a 'hydrogen bond':



this stabilizes the ion relative to the acid and so increases the strength of the acid. In fumaric acid the carboxyl groups are farther apart; the electrostatic effect is smaller and so fumaric acid is considerably weaker than maleic acid.

It is interesting to compare the effect that substituents have on the strength of acids with their effect on the rate of $-S_1$ replacement reactions, since both are ionization processes. The strength of an acid depends on the relative stabilities of it and its conjugate base, the rate of a $-S_1$ replacement on the relative stabilities of the initial and transition states. In each case the effect of the substituent depends on whether it stabilizes the initial uncharged compound more or less than the charged ion or transition state. There is therefore an exact parallel between the effect of substituents on the two reactions, but of course the signs of the charges differ in the two cases; for example, —I substituents weaken acids but increase the rate of $-S_1$ replacements.

Relation between structure and strength in bases

A similar consideration of the reaction of a base (B) with an acid (HA),

$$B + HA \rightarrow BH^+ + A^-$$

leads to the conclusion that the base should be stronger

(1) the greater the H—B bond-energy;
(2) the smaller the ionization potential of B;
(3) the greater the resonance energy of HB^+ compared with that of B.

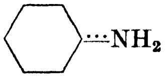
These effects are exactly the converse of those determining the strengths of acids, as they must be, since the strength of a base B varies inversely as the strength of its conjugate acid HB^+. Once again the bond-energy effect is usually unimportant. The effect of changing ionization potential is seen in the series CH_3^-, NH_2^-, OH^-, F^-, where the basic strength falls as the ionization potential increases. The effect of substituents in altering the ionization potential of the central atom is well shown by the greater basic strengths of amines compared with ammonia; —I substituents lower the ionization potential of nitrogen. The effect of a +I substituent is well shown in Table 15, the CN and RO substituents producing a marked decrease in basicity.

TABLE 15

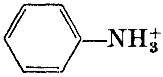
Base	pK_B
NH_3	4·75
$NH_2 \cdot NH_2$†	5·8
NH_2OH	8·0
Me_2NH	3·3
Et_2NH	3·0
$Et_2N \cdot CH_2OEt$	7·7
$Et_2N \cdot CH_2CN$	10

† Showing that NH_2 is a +I group.

The effects of mesomerism on basic strengths are also very striking. We may divide them into three categories. In the first, the base is mesomeric but the salts less so, because addition of a proton removes a pair of electrons from the mesomeric system. Aniline is mesomeric (I), but anilinium salts less so since in the anilinium ion (II) the nitrogen no longer has free *p*-electrons available for *π*-bond formation. In such cases the free base has a larger resonance energy than the salt and so the mesomerism reduces the basicity of the former. (This effect is seen even more strikingly in pyrrole which is almost non-basic, for in the corresponding salts the large resonance energy of the aromatic ring would be lost.) The basicity of nitrogen is therefore lowered by adjacent +E substituents. Examples are given in the following table.

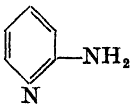


(I)

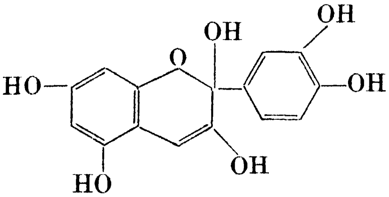


(II)

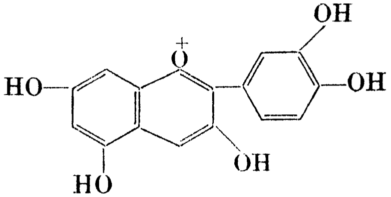
TABLE 16

Base	pK_B
NH_3	4·75
$Ph \cdot NH_2$	9·4
$CH_3CO \cdot NH_2$	14·5
$CO(NH_2)_2$	14·8
$CS(NH_2)_2$	15·0
	7·5

The second category contains compounds whose basicity is greatly increased by the fact that they themselves are not mesomeric while their salts are. The best examples are provided by the anthocyanidins. The oxygen-containing ring in cyanidin base (III) is not mesomeric, but in cyanidin salts (IV) it is actually aromatic; therefore the latter are greatly stabilized relative to the former and so cyanidin salts are stable, although simple oxonium salts have been isolated only in exceptional cases.

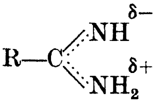


(III)



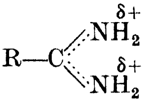
(IV)

The third category contains compounds in which the basic centre forms part of a mesomeric system, but the mesomerism is made possible only by a separation of charges. Addition of a proton gives a cation in which mesomerism involves a spreading of charge only. The latter process is energetically much more favourable than charge-separation and so the ion is more degenerate and has a larger resonance energy than the base; the strength of the base is thereby increased. Amidines provide a simple example; amidines are mesomeric (V), but only by a separation of charge to give a zwitterion. In the amidinium ion (VI) there is no separation, only a spreading of charge. Amidines are very strong bases. The same is true of guanidines and of the amidine analogue[†] (VII) which gives mesomeric salts containing the ion (VIII).



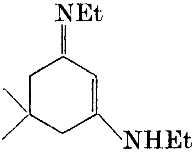
$$R{-}C\begin{smallmatrix}\cdot\overset{\delta-}{NH}\\ \cdot\overset{\delta+}{NH_2}\end{smallmatrix}$$

(V)

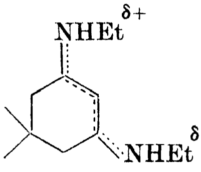


$$R{-}C\begin{smallmatrix}\cdot\overset{\delta+}{NH_2}\\ \cdot\overset{\delta+}{NH_2}\end{smallmatrix}$$

(VI)

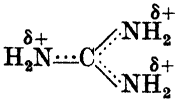


(VII)



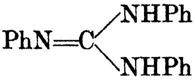
(VIII)

Guanidine is a particularly strong base since the cation (IX) is completely symmetrical and has a very large resonance energy. It is interesting that unsymmetrical alkylguanidines are weaker bases than guanidine although the —I effect of the alkyls might have been expected to increase the basicity; this effect is overbalanced by the decrease in resonance energy due to the decrease in symmetry. It is also noteworthy that *sym*-triphenylguanidine (X) is a very strong base although one might have expected the +E phenyl groups to lower the basicity of the nitrogen atoms greatly. Here again the symmetry of the triphenylguanidinium ion is decisive. Mono- and diphenylguanidine are relatively weak bases.



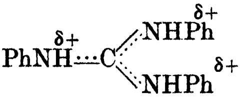
$$\overset{\delta+}{H_2N}\cdots C\begin{smallmatrix}\cdot\overset{\delta+}{NH_2}\\ \cdot\overset{\delta+}{NH_2}\end{smallmatrix}$$

(IX)



$$PhN{=}C\begin{smallmatrix}NHPh\\ NHPh\end{smallmatrix}$$

(X)

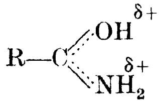


$$\overset{\delta+}{PhNH}\cdots C\begin{smallmatrix}\cdot\overset{\delta+}{NHPh}\\ \cdot\overset{\delta+}{NHPh}\end{smallmatrix}$$

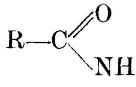
(XI)

[†] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1162.

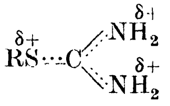
The relatively high basicity of amides, urea, and their sulphur analogues have a similar origin. In their salts the proton must be bound to oxygen or sulphur, giving mesomeric ions (e.g. XII), rather than to nitrogen, giving products (e.g. XIII) where even the resonance energy of the parent base would be wholly or partly lost. The formation of S-alkyl*iso*thiourea salts (XIV) from thiourea and alkyl halides, in preference to the N-alkyl isomers, is another example of the same effect. So too is the fact that carboxylic acids are almost as strongly basic as ketones (Table 1), although one might expect the basicity of the carbonyl in acids to be greatly lowered by the presence of the +I hydroxyl; this effect is counterbalanced by the greater resonance energy of the cation (XV) compared with that of the parent acid.



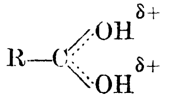
(XII)



(XIII)

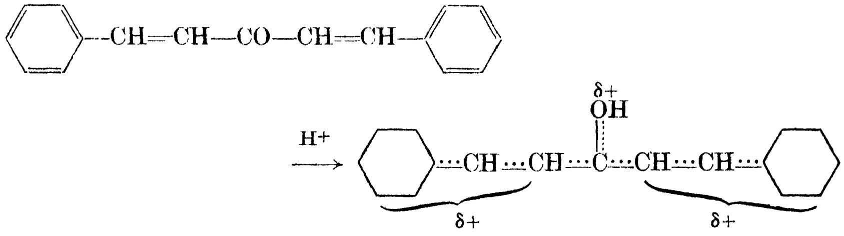


(XIV)

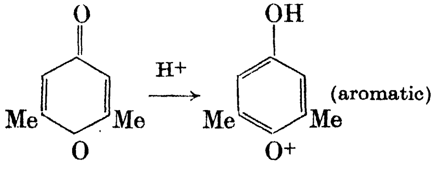


(XV)

The relatively high basicity of many unsaturated ketones may also be ascribed to the fact that mesomerism of their salts does not involve charge separation; dibenzalacetone (XVI) and 2:6-dimethyl-γ-pyrone (XVII) are good examples. The increased mesomerism of the salts of the former is shown by the fact that they absorb light of larger wavelength than does the free base, and so salt-formation takes place with a deepening of colour (halochromism: see Chapter XIV).



(XVI)



(XVII)

Acid-base catalysis

Many reactions are known in which a reactant must first be converted to a salt, either by loss or gain of a proton. Such reactions do not occur in the absence of an appropriate proton sink or source, that is, in the absence of appropriate basic or acidic catalysts. The base-catalysed reaction of a compound HX with Y may be represented:

$$HX + B \rightarrow X^- + BH^+ \qquad (1)$$

$$X^- + BH^+ \rightarrow HX + B \qquad (2)$$

$$X^- + Y \rightarrow \text{products.} \qquad (3)$$

Reactions (1) and (2) represent the reversible formation of the intermediate ion X^-. This kinetic scheme is identical with the one discussed on p. 21, and it follows that the overall rate of reaction to form the products (P) is

$$\frac{d[P]}{dt} = \frac{k_1 k_3 [HX][B][Y]}{k_2 + k_3 [Y]}.$$

There are two main cases. If salt-formation is rapid, that is, if k_1 and k_2 are large, the second term in the denominator is negligible and the rate will be approximately

$$\frac{d[P]}{dt} \simeq \frac{k_1 k_3}{k_2}[HX][B][Y].$$

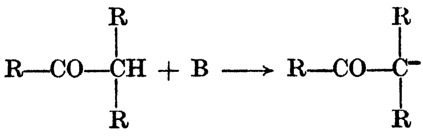
The rate of reaction will be determined by the dissociation constant of HX and the rate of reaction (3). No new principles will be involved, since the dependence of acid strength on structure has already been discussed, while the third reaction will be quite normal. The overall rate will depend on the concentrations of both reactants and of the catalyst. A good example is the acid-catalysed hydrolysis of esters (p. 120). If, on the other hand, the third reaction is fast compared with the first two, it is the first term in the denominator which becomes negligible, and the rate of reaction is then approximately

$$\frac{d[P]}{dt} \simeq k_1 [HX][B],$$

that is, equal to that of the first (rate-determining) step. The rate of reaction is then independent of the concentration of one reactant (Y), and depends only on the speed with which HX is converted to its salt by the basic catalyst. Reactions of this type, where the rate-determining step is a proton transfer, are called *prototropic.* A similar analysis applies also to acid-catalysed reactions, but true prototropy is there of little importance. Very few bases are known which do not react rapidly with ordinary acids.

Prototropic reactions

The simplest types of prototropic reaction are those in which the intermediate anion reacts with a cationoid reagent to form a stable product. Three such processes involving ketones have been examined in detail. In all of them the ketone is first converted to its conjugate anion by the basic catalyst.



$$R{-}CO{-}CHR_2 + B \longrightarrow R{-}CO{-}CR_2^-$$

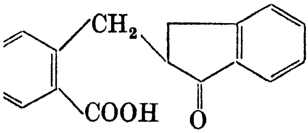
In the first the ion reacts with a halogen to give a haloketone, e.g.:

$$R—CO—CR_2^- + Br\cdot Br \rightarrow R—CO—CR_2Br + Br^-.$$

In the second the ion reacts with a deuterium ion to form a deuterated ketone:

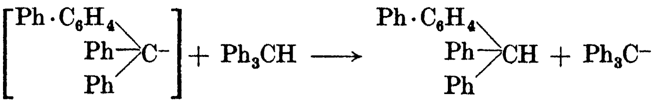
$$R—CO—CR_2^- + D^+ \rightarrow R—CO—CR_2D.$$

In the third the initial ketone is optically active; the anion, however, racemizes readily since it can pass into a symmetrical planar form analogous to free methyl (p. 7). The anion adds a proton to regenerate an optically inactive form of the original ketone. The rates of these reactions are found to depend on the concentrations of the ketone and basic catalyst only; hence the rate-determining step must be the production of an intermediate from them, and this step can hardly be other than the ionization of the ketone. A particularly pleasing proof of the mechanism has been given by Hsü, Ingold, and Wilson,† who showed that in the case of the optically active ketone



the rates of base-catalysed bromination, deuteration, and racemization were all identical, implying that the rate-determining step in all three reactions is the same.

The idea that ionization might be a slow process used to be heretical in the days when views were coloured by the ionic reactions of inorganic chemistry which are generally extremely fast. It was then suggested that prototropic reactions of ketones might involve preliminary isomerization of the ketone to its enol by some unspecified catalytic action of the alkali, the enol then ionizing rapidly. This *ad hoc* hypothesis became unnecessary when slow ionic reactions were discovered by inorganic chemists, and it is now generally recognized that ionization may be a very slow reaction. Indeed, Conant and Wheland‡ have shown that prototropic reactions of the type



$$\left[\begin{array}{l} Ph\cdot C_6H_4\diagdown \\ \quad Ph\!>\!C^- \\ \quad Ph\diagup \end{array}\right] + Ph_3CH \longrightarrow \begin{array}{l} Ph\cdot C_6H_4\diagdown \\ \quad Ph\!>\!CH \\ \quad Ph\diagup \end{array} + Ph_3C^-$$

are often very slow, being half complete at room temperature only after hours or even days. Here there can be no question of intermediate enolization.

Numerous other protropic reactions are known, many of which will be discussed later in this chapter and elsewhere throughout the book. All follow the same general principles although few, it is true, have been studied kinetically. For instance, nitro-compounds, e.g. nitromethane, and sulphones undergo the same base-catalysed reactions (halogenation, etc.) as do ketones.

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† *J.C.S.* 1936, 623; 1938, 78.

‡ *J.A.C.S.* 1932, **54**, 1212.

Relation between structure and rate in prototropic reactions

Only base-catalysed prototropic reactions need be considered since they are much the more important and better understood. For the rate of such a reaction to be measurable and yet governed by the proton transfer, it is necessary that the proton transfer be slow. This condition is only fulfilled by compounds in which the hydrogen is attached to carbon; removal of a proton from oxygen or nitrogen by bases is almost always too fast to measure.† On the other hand, the activation energy must be at least as great as the heat of ionic dissociation of the hydride. This heat of dissociation is very large in paraffin hydrocarbons and so such compounds cannot undergo prototropic reactions at measurable speed. Prototropy is virtually confined to carbon derivatives where the rate of ionization of CH is increased by suitable substitution.

The transition state of the reaction $HA+B \rightarrow A^{-}+BH^{+}$ may be written:

$$\overset{\delta-}{A}\cdots H\cdots\overset{\delta+}{B}.$$

For reactions involving the same basic catalyst, the rate will then be increased by substituents in A which stabilize the transition state. Since A is more negative in the transition state than in the initial state, the former will be stabilized by substituents which increase the electron-affinity of A. Therefore +I substituents in A will increase the rate and conversely —I substituents will reduce it. Moreover, the weakening of the AH bond in the transition state makes its electrons available for conjugation with +E substituents in A, and the negative charge on A in the transition state will facilitate such conjugation. Therefore +E substituents in A will accelerate the proton transfer. In practice the E-effect is again of dominant importance, and prototropy is observed only in compounds of the type X—C—H, where X is a +E substituent, e.g. RCO, NO_2, RSO_2, CN, etc.

In a compound of this type the rate may be modified by further substituents, being increased by +I or +E substituents and retarded by —I. That —I alkyl substituents do lower the rate of dissociation is shown by the relative rates of salt-formation of nitroparaffins with alkali, and of base-catalysed bromination of acetophenone derivatives (Table 17). The effect of positive substituents is shown by the much greater ease of base-catalysed bromination in malonic ester than in acetic ester, and in acetoacetic ester than in acetone; in each case the second +E substituent increases the rate of dissociation. The effect of +I substituents is well seen in the base-catalysed bromination of acetone, where *as*-tribromacetone, CH_3—CO—CBr_3, is the first isolable product; presumably mono- and dibromacetone are intermediates, but in each the +I bromine increases the rate of ionization and so both brominate more rapidly than acetone. Therefore the monobromacetone is converted to tribromacetone as soon as it is formed.

---

† There are several possible explanations for this difference, but the actual reason is still uncertain.

TABLE 17

	Relative rates of neutralization†		*Relative rates of bromination*‡
$CH_3\cdot NO_2$	1	$Ph\cdot CO\cdot CH_3$	1
$Me\cdot CH_2\cdot NO_2$	0·164	$Ph\cdot CO\cdot CH_2Me$	0·154
$Et\cdot CH_2\cdot NO_2$	0·123	$Ph\cdot CO\cdot CH_2Et$	0·120
$Me_2CH\cdot NO_2$	0·0087	$Ph\cdot CO\cdot CH_2Pr_\beta$	0·059
		$Ph\cdot CO\cdot CHMe_2$	0·030

† Junell, *Diss.*, Upsala, 1935; Maron and La Mer, *J.A.C.S.* 1938, **60**, 2588.
‡ Evans and Gordon, *J.C.S.* 1938, 1434.

Substituents which increase the rate of prototropic reaction in a hydride also increase its acidity; for in one case they stabilize $A^{\delta-}$ in the transition state, in the other A^- in the product, and both these differ from the initial state in qualitatively the same manner (negative charge and electrons available for conjugation).

Prototropic tautomerism

It is always possible to write two or more classical structures for a mesomeric anion in which the negative charge is spread over two or more atoms; when such an anion combines with a proton to form a non-mesomeric acid, it can do so in at least two different ways to give products corresponding to the classical forms of the ion. The resulting acids are chemically distinct and not merely forms in a resonance hybrid, since they differ in the position of one atomic nucleus. Both will, however, give the same mesomeric anion with bases. Therefore bases will catalytically convert either acid into an equilibrium mixture of the two; the acids will therefore be tautomeric, and the phenomenon of tautomers differing only in the location of bonds, and of one hydrogen atom, and interconvertible through a common mesomeric anion, is called *prototropic tautomerism.*

If the acids are written as HA and AH and the base as B, the equilibria to be considered are

$$HA + B \rightleftharpoons A^- + BH^+ \rightleftharpoons AH + B.$$

We have $$\frac{[A^-][BH^+]}{[HA][B]} = K_1, \quad \frac{[A^-][BH^+]}{[AH][B]} = K_2,$$

whence $$\frac{[HA]}{[AH]} = \frac{K_2}{K_1} = K.$$

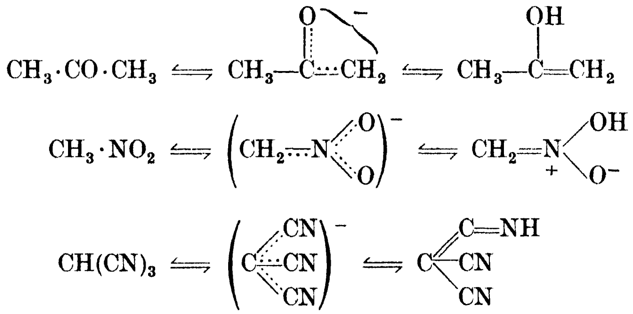
This equilibrium is therefore independent of [B], as of course it must be, the action of the base being purely catalytic.

Moreover, if $B \equiv H_2O$, we have

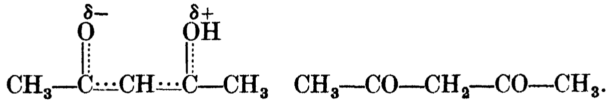
$$\frac{[HA]}{[AH]} = K \equiv \frac{K_{AH}}{K_{HA}},$$

where K_{AH}, K_{HA} are the dissociation constants of the two acids. The position of equilibrium therefore depends on the relative acid strengths of the tautomers, the weaker acid being favoured at equilibrium.

The most interesting cases of prototropic tautomerism are those in which at least one form is interconverted to the common ion at measurable speed; that is to say, where the hydrogen is attached to carbon in at least one tautomer. Any compound of the type $H—CR_2—X$, where X is a +E group, will come into this category since the ion $^-CR_2—X$ will be mesomeric. Some examples of such tautomerism are given below:



No special discussion of these reactions is necessary. The rates of interconversion depend on rates of ionization and the variation of these with structure follows the principles already laid down. The equilibrium between keto and enol forms depends on their relative acid strengths, and the effect of structure on acid strength has already been considered.† Thus introduction of a second +E group into acetone, giving acetylacetone, greatly increases the rate of ionization of the keto form. Moreover, enol acetylacetone is itself conjugated while the keto form is not:



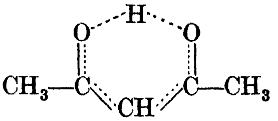
$$CH_3—\overset{\overset{\delta-}{O}}{C}\cdots CH\cdots\overset{\overset{\delta+}{OH}}{C}—CH_3 \quad CH_3—CO—CH_2—CO—CH_3.$$

This mesomerism stabilizes the enol form relative to the keto and so lowers its relative acid strength. Therefore in acetylacetone the enol form is present in higher concentration at equilibrium than is the case in acetone.

---

† Other things being equal, a ketone is more stable than the corresponding enol, because the sum of the bond-energies in H—C—C=O is greater than that in C=C—O—H.

(It is quite possible that in the enol form resonance takes place by chelation,



but clearly this would not affect the argument.)

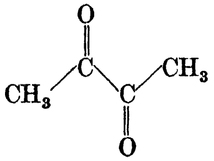
The effect of additional +E substituents on the position of equilibrium is shown by the following classical results of Meyer,[†] the +E effects of the various groups being in the order:

$$\mathrm{MeOOC\cdot CO > Ph\cdot CO > Me\cdot CO > MeOOC.}$$

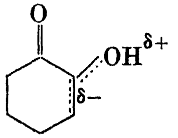
Substance	*% enol in* EtOH
$\mathrm{Me\cdot CO\cdot CH_2\cdot COOMe}$	4·8
$\mathrm{Me\cdot CO\cdot CH_2\cdot CO\cdot Me}$	80·4
$\mathrm{Me\cdot CO\cdot CH_2\cdot CO\cdot Ph}$	98·0
$\mathrm{Ph\cdot CO\cdot CH_2\cdot COOMe}$	26
$\mathrm{MeOOC\cdot CO\cdot CH_2\cdot COOMe}$	100
$\mathrm{(Me\cdot CO)_3CH}$[‡]	89

The concentrations of enol at equilibrium for acetone and methyl acetate are very small ($2{\cdot}5\times 10^{-4}$ per cent. for acetone; p. 103, ref. †).

A very interesting application of the general principles has been cited by Wheland.[§] Open-chain 1:2-diketones, e.g. diacetyl, exist almost entirely in the keto form since the effect of the group R·CO·CO on the acidity of C—H differs little from that of R·CO. On the other hand, diosphenols, i.e. cyclic 1:2-diketones, are largely enolic. Now the open-chain diketones will occur almost exclusively in the *trans* form owing to the mutual repulsion of the C=O dipoles:



in the cyclic ketones, e.g. 1:2-cyclohexandione, the carbonyls are constrained by the ring to adopt a *cis* configuration. Since in the enol form one of the strongly polar C=O bonds is replaced by a less polar C—O, and since the negative charge on the oxygen is still further reduced by mesomerism, viz.



[†] *Annalen*, 1911, **380**, 212; *Ber.* 1911, **44**, 2725; 1912, **45**, 2843.

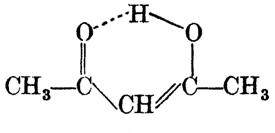
[‡] Seidel, Thier, Uber, and Dittmer, *Ber.* 1936, **69**, 650.

[§] *J. Chem. Phys.* 1933, **1**, 731.

the O—O repulsion is smaller in the enol and so it is stabilized relative to the keto form.†

Effect of solvent on equilibrium

Although the keto-enol equilibrium in a given solvent will be independent of the basic catalyst, it will be affected by a change of solvent. The carbonyl group in a ketone is much more polar than the C=C—OH system in an enol, particularly in compounds like acetylacetone where hydrogen bonding in the enol is possible.



An increase in dielectric constant of the solvent will therefore favour the keto form, the increase in solvation energy being greater for the more polar isomer. This effect is shown very strikingly by the different equilibrium concentrations of enol in alcohol and in the gas phase, the latter corresponding to a solution in a solvent of unit dielectric constant (Table 18).

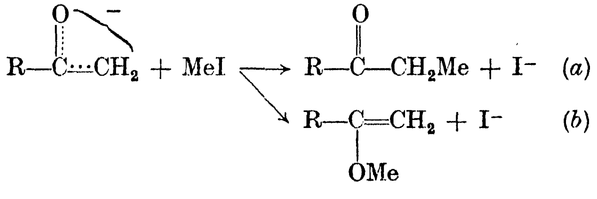
Table 18

Compound	*% enol in* EtOH	*% enol in vapour*‡
$CH_3 \cdot CO \cdot CH_2 \cdot COOEt$	10	46
$CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$	83	92
$CH(COOMe)_3$	Very small	12

‡ Conant and Thompson, *J.A.C.S.* 1932, **54**, 4039.

Reactions of mesomeric anions

Just as a mesomeric anion can combine with a proton in two or more different ways, so also can it give alternative products with other cationoid reagents. Thus an enolate ion with MeI can give either C- (*a*) or O-methyl (*b*) derivatives:



The situation is complicated by the fact that the proportion of isomers varies with the cationoid reagent; the general explanation§ seems to be this.

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† Recently the equilibria have been investigated by Schwarzenbach and Wittwer, *Helv. Chim. Acta*, 1947, **30**, 663, who find that, in alcoholic solution, 1:2-cyclohexandione is 70 per cent. enolic, 1:2-cyclopentandione 100 per cent. enolic.

§ This argument was suggested by Birch and developed in more detail by Dewar, at a recent Faraday Society Discussion on the Labile Molecule (Oxford, September 1947).

The rate of addition will vary with the collision frequency and the entropy and energy of activation. Now a cationoid reagent will collide most frequently with that atom in a mesomeric anion which carries the largest net negative charge; and the entropy of activation will be least for the reaction which leads to least displacement of nuclei in the anion. Thus the temperature-independent factor (A_b) for formation of an enol derivative from an enolate ion is larger than the corresponding factor (A_a) for ketone formation; because in the ion the charge resides mainly on oxygen and the structure already approximates to C═C—O⁻.

But the activation energy may be greater for the reaction so favoured. Thus the total binding energy of a ketone is greater than that of the corresponding enol (p. 101), and so the transition state for ketone formation should be likewise the more stable; it contains a partial C═O π-bond, whose bond-energy is greater than that of the partial C═C π-bond in the enol transition state.

Therefore the velocity constants for ketone and enol formation are given by

$$K_{\text{ketone}} = A_a e^{-E_a/RT}$$
$$K_{\text{enol}} = A_b e^{-E_b/RT},$$

where $A_a < A_b$, $E_a < E_b$. The ratio of rates is therefore given by

$$\frac{K_{\text{ketone}}}{K_{\text{enol}}} = \frac{A_a}{A_b} e^{E_b-E_a/RT}.$$

Now the difference in activation energies ($E_b - E_a$) will presumably be roughly proportional to their absolute magnitudes. Therefore for very active cationoid reagents, i.e. compounds combining with the anion with low activation energies, $E_b - E_a$ will be small; the ratio of rates is then determined largely by the ratio A_a/A_b, and so enol is preferentially formed. But for a cationoid reagent of low activity, the difference $E_b - E_a$ will be large; the exponential factor will then outweigh the difference in the A's, and so ketone is formed more rapidly.

It is indeed found that active cations such as H^+ and acyl$^+$ (in the form of acyl pyridinium salts) gives enol derivatives with enolate ions, while weak cationoid reagents such as MeI give ketones.

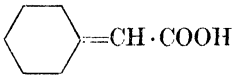
Similar considerations should apply in the case of other mesomeric ions (see Birch, p. 103, for examples). Incidentally the exponential term should vary with temperature, so the proportions of enol and ketone derivatives should be temperature-dependent. Here no such effect has been observed, but addition to certain allyl anions (p. 282) shows the expected relation.

Three-carbon tautomerism

A special case of prototropic tautomerism of great importance is the interconversion of allyl derivatives; e.g.:

$$R\cdot CH{=}CH{-}CH_2R' \rightleftharpoons R\cdot CH_2{-}CH{=}CH\cdot R'.$$

The main differences from the cases already considered are that in allyl systems both tautomers are interconverted slowly to the common ion, and that additional +E substituents must be present to increase the rates of ionization sufficiently for them to be measurable, i.e. to make the system 'mobile'. Thus olefines are not rearranged by bases since their acidity is too small; but if a +E substituent is present rearrangement becomes possible. The mobility of the system is increased by further positive substituents or an increase in +E activity of the original activating group. For instance, the acids



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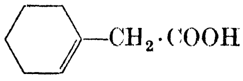
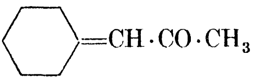


are only interconverted slowly by hot alkali; but their esters are more labile and the corresponding ketones



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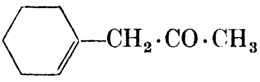
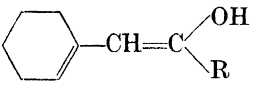


are interconverted so readily that isolation of the pure isomers is difficult. The +E activity of the substituents rises in the series:

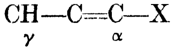
$$—COOH < —COOR < —CO·CH_3.$$

Strictly, of course, both isomers should also be in equilibrium with an enol form



but, as in acetone, the concentration of enol at equilibrium is negligible.

The proportions of the two forms at equilibrium follow the general principle that the less basic is favoured, but the usual treatment of the problem is quite unsound.† We may discuss the system



$$\underset{\gamma}{\mathrm{CH}}—\mathrm{C}{=}\underset{\alpha}{\mathrm{C}}—\mathrm{X}$$

where X is the +E activating group. A positive α-substituent will increase the acidity of the α-CH form and so decrease the concentration of the $\beta{:}\gamma$ unsaturated isomer at equilibrium. Similarly a positive γ-substituent will favour the $\beta{:}\gamma$ unsaturated form. The effect of a —I α-substituent is less predictable; such a substituent will lower the acidity of the adjacent carbon and should therefore favour the form with the mobile hydrogen attached to that carbon. On the other hand, such substituents (e.g. Me) can hyperconjugate with the double bond in the $\alpha{:}\beta$ unsaturated form and so stabilize it. The latter effect predominates, and so a methyl in the α-position favours the $\alpha{:}\beta$, in the γ-position the $\beta{:}\gamma$ unsaturated isomer. In the β-position substituents will affect the acidity of both α- and γ-positions equally. But groups capable of exerting a —E effect by conjugation (e.g. Ph) or hyperconjugation (e.g. Me) will stabilize the $\alpha:\beta$ unsaturated form since in it alone the substituent can conjugate with the terminal group X through the double bond. These principles are well illustrated by the results of Kon, Linstead, and their collaborators† on the equilibria between vinylacetic and crotonic acids. The difference between acids 3 and 8 is particularly revealing; the —E effect of ethyl due to hyperconjugation is less than that of methyl.

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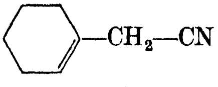
† Cf. Baker (*Tautomerism*, Routledge, 1934), who, however, gives a useful survey of the experimental data.

	$\beta:\gamma$ unsaturated isomer	% *$\alpha:\beta$ at equilibrium in alkali*
1.	$H_2C{=}CH{\cdot}CH_2{\cdot}COOH$	100
2.	$MeCH{=}CH{\cdot}CH_2{\cdot}COOH$	75·4
3.	$Me_2C{=}CH{\cdot}CH_2{\cdot}COOH$	5·6
4.	$MeCH{=}CH{\cdot}CHMe{\cdot}COOH$	80·7
5.	$MeCH{=}CMe{\cdot}CH_2{\cdot}COOH$	26
6.	$MeCH{=}CPh{\cdot}CH_2{\cdot}COOH$	25
7.	$Me_2C{=}CPh{\cdot}CH_2{\cdot}COOH$	54
8.	$MeEtC{=}CH{\cdot}CH_2{\cdot}COOH$	23

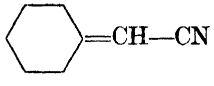
Rates of ionization of tautomers

At equilibrium the less acidic tautomer is favoured. In a 3-carbon system the rates of ionization of the isomers will follow the usual principles, that a CH bond ionizes more readily the greater its acid strength. Therefore the more stable form is also converted the more slowly to the equilibrium mixture by bases. A further interesting point has been raised by Ingold, de Salas, and Wilson.‡

The nitrile (XVIII)

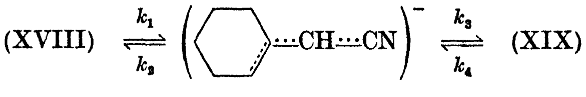


(XVIII)



(XIX)

exchanges both hydrogen atoms α to CN too rapidly for measurement under conditions where the half-life of conversion into (XIX) is 7 hours. At equilibrium (XIX) is greatly favoured, but evidently the less stable isomer is regenerated the more rapidly from the common ion. If we consider the rates of the various reactions:



this result shows that $k_2 > k_3$. The predominance of (XIX) at equilibrium implies that $k_3/k_4 > k_2/k_1$. The two conditions are compatible. The less stable isomer is interconverted more rapidly to the ion, but the rate of ionization (k_4) of (XIX) is so small that it is favoured at equilibrium.

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† *J.C.S.* 1926, 2748; 1927, 355; 1928, 2343; 1929, 2498; 1930, 1603, 2064; 1931, 1411; 1932, 2452.

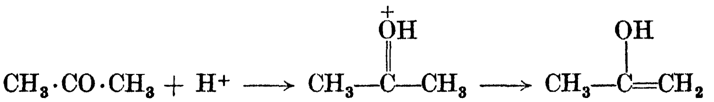
‡ Ibid. 1936, 1328.

Pseudo-acids

This result throws light on the phenomenon of pseudo-acidity. Many compounds are known which appear to show no appreciable acidity, but dissolve slowly in alkali to form true salts. On acidification, an *aci* isomer of the original compound is obtained which forms salts rapidly with bases, but slowly reverts to the original 'non-acidic' compound. Nitromethane is a typical example. Classical organic chemists therefore supposed that the salts were derived from the *aci* form, but it is now clear that the phenomenon is merely one of prototropic tautomerism where the common ion is more rapidly converted to the less stable tautomer by acid. In most cases the mobile hydrogen is attached to oxygen or nitrogen in the *aci* form and so its rate of ionization is very great; but cyclohexenylacetonitrile (XVIII) would be a typical pseudo-acid in the classical sense. Incidentally the classical assumption that *aci* forms are always the more acidic is incorrect. Thus at equilibrium in alcohol, triacetylmethane ($CH(COCH_3)_3$) is present mainly as enol; it therefore follows from the general theory that the keto isomer, although it forms salts more slowly with bases, is actually the stronger acid.

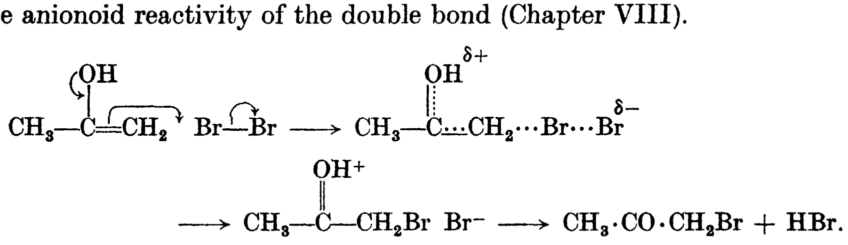
Acid-catalysed prototropy

The majority of prototropic reactions can be catalysed by acids as well as by bases. Under these conditions the compound first adds a proton at one point and then loses a proton from some other point to form a reactive tautomer. Thus acetone can be halogenated in presence of acids; the acetone first forms a salt which gives enol acetone by loss of a proton.



$$CH_3\cdot CO\cdot CH_3 + H^+ \longrightarrow CH_3\text{—}\overset{\overset{+}{O}H}{\overset{\|}{C}}\text{—}CH_3 \longrightarrow CH_3\text{—}\overset{OH}{\overset{|}{C}}{=}CH_2$$

The enol then reacts rapidly with halogen, the —E hydroxyl increasing the anionoid reactivity of the double bond (Chapter VIII).



$$CH_3\text{—}\overset{OH}{\overset{|}{C}}{=}CH_2\ \ Br\text{—}Br \longrightarrow CH_3\text{—}\overset{\overset{\delta+}{OH}}{\overset{\vdots}{C}}\cdots CH_2\cdots Br\cdots \overset{\delta-}{Br}$$

$$\longrightarrow CH_3\text{—}\overset{OH^+}{\overset{\|}{C}}\text{—}CH_2Br\ \ Br^- \longrightarrow CH_3\cdot CO\cdot CH_2Br + HBr.$$

Since the carbonyl group is an extremely weak base, ketones are only converted to their salts to a minute extent under ordinary conditions of acid catalysis; the rate of reaction therefore depends mainly on the amount of ketone salt present rather than on its reactivity. Substituents (—I) which increase the basicity of the ketone will therefore increase the rate of reaction. Conversely +I substituents will decrease the rate. Thus bromoacetone is a weaker base than acetone, and 1:1-dibromoacetone weaker still. When acetone is brominated in presence of acid, the intermediate bromo derivatives can therefore be isolated, since they react more slowly than acetone; while in the base-catalysed reaction *as*-tribromoacetone is the first isolable product (p. 100).

Miscellaneous prototropic reactions

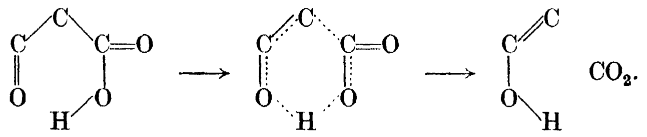
1. *Decarboxylation*

A number of carboxylic acids readily lose carbon dioxide on heating. Recent work has shown that they can be divided into two types. In the first it is the anion which decarboxylates, giving an ion whose mesomeric stabilization provides the driving force for the reaction. A good example is triphenylacetic acid:

$$Ph_3C{\cdot}COOH \rightarrow Ph_3C{\cdot}COO^- + H^+$$
$$Ph_3C{\cdot}COO^- \rightarrow Ph_3C^- + CO_2;$$

α-picolinic acid is another (cf. p. 115). Since ionization is a necessary preliminary, decarboxylation occurs more readily in solvents of high dielectric constant.

A second group of acids, of which β-ketoacids are the most important, decarboxylate at much the same rate in different solvents, showing that ionization is not involved in the reaction.† Here hydrogen bonding plays a dominant role, the mechanism apparently being:



2. *Decomposition of acids by* H_2SO_4

Triphenylacetic acid, with concentrated sulphuric acid, gives carbon monoxide, water, and triphenylcarbonium sulphate. The reaction evidently involves a prototropic removal of the hydroxyl, and the resulting triphenylacetyl cation simultaneously loses CO to form the mesomeric Ph_3C^+ ion.

$$Ph_3C\text{—}CO\text{—}OH\ H^+ \rightarrow Ph_3\overset{\delta+}{C}\cdots CO\cdots OH\cdots\overset{\delta+}{H}$$
$$\rightarrow Ph_3C^+\ CO\ \ OH_2.$$

This reaction also occurs in other acids $R{\cdot}COOH$ if R^+ is stable. Thus formic acid gives the reaction ($R^+ \equiv H^+$) and so does oxalic acid:

$$R^+ = (COOH)^+ = CO_2 + H^+.$$

So, too, do α-hydroxy acids, the positive charge on the product being located on a relatively basic oxygen atom:

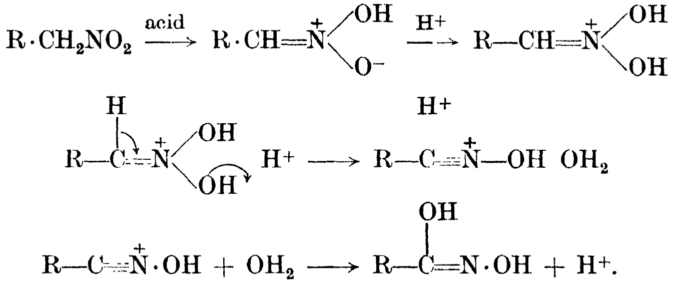
$$H\text{—}OCR_2\text{—}CO\text{—}OH\ H^+ \rightarrow \overset{\delta+}{HO}\cdots CR_2\cdots CO\cdots OH\cdots\overset{\delta+}{H}$$
$$\rightarrow H\overset{+}{O}{=}CR_2\ \ CO\ \ OH_2.$$

---

† Westheimer and Jones, *J.A.C.S.* 1941, **63**, 3283.

3. *Primary nitro-compounds*

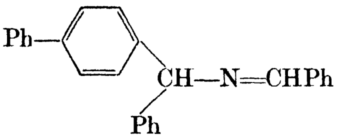
On treatment with hot strong (50 per cent.) sulphuric acid, compounds of the type $R\cdot CH_2\cdot NO_2$ give carboxylic acids and hydroxylamine, a reaction of considerable technical importance. The first step is undoubtedly an acid-catalysed conversion of the nitro-compound to its *aci* form and the subsequent reactions are probably as follows:



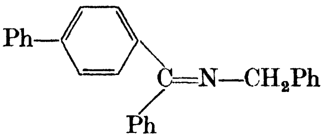
The hydroxamic acid so formed is rapidly hydrolysed to hydroxylamine and a carboxylic acid.

S_2 prototropic tautomerism

In the normal interconversion of prototropic tautomers by bases, each is first converted to the common ion which subsequently acquires a proton; the process is analogous to an S_1 replacement. One case is known, however, where the whole reaction takes place in one single step, being therefore of the S_2 type. Optically active Schiff bases such as (XX)

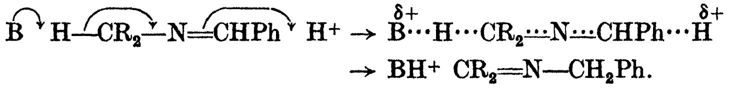


(XX)



(XXI)

are racemized by alkali and are simultaneously converted into equilibrium mixtures with their tautomers, e.g. (XXI). It is possible to measure the actual rate of conversion of (XX) into (XXI) and this is found to be equal to the rate of racemization. Now, if the reaction proceeded through a common ion, the common ion would regenerate an equilibrium mixture of (XX) and (XXI), both inactive of course. Therefore the rate of formation of (XXI) from (XX) would be less than the rate of ionization of (XX), that is, less than the rate of racemization. The experimental results† show, however, that every time (XX) reacts with alkali, it is converted into (XXI); this can only mean that addition and removal of the proton take place simultaneously.



$$B\ H{-}CR_2{-}N{=}CHPh\ H^+ \rightarrow \overset{\delta+}{B}\cdots H\cdots CR_2\cdots N\cdots CHPh\cdots\overset{\delta+}{H} \rightarrow BH^+\ CR_2{=}N{-}CH_2Ph.$$

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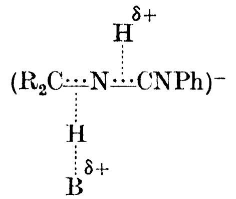
† Hsü, Ingold, and Wilson, *J.C.S.* 1935, 1778; Ingold and Wilson, ibid. 1934, 93.

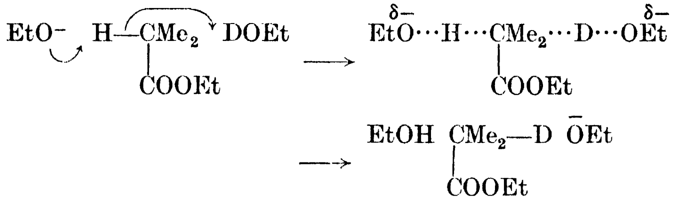
At first sight one might suppose that this mechanism would conflict with the arguments levelled against its anionotropic counterpart (p. 85); but here the number of electrons in the system is smaller and so the two protons in the transition state can be linked by molecular bonds to the common ion, which has a favourable electronic and stereochemical configuration.



$$\overset{\overset{\delta+}{H}}{\vdots}\qquad (R_2C\cdots N\cdots CNPh)^- \quad \underset{\underset{B}{\vdots\,\delta+}}{\overset{\vdots}{H}}$$

In the anionoid reaction such an intermediate would not be possible.

A similar explanation probably holds for the sodium ethoxide catalysis of deuterium exchange in ethyl *iso*-butyrate; since sodium ethoxide is not a sufficiently powerful base to effect Claisen condensations with this ester (p. 128), it is likely that the exchange takes place by an S_2 mechanism.



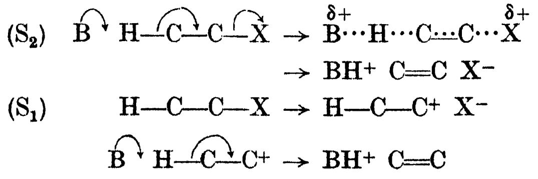
$$EtO^- \; H\text{—}\underset{COOEt}{CMe_2}\; DOEt \longrightarrow \overset{\delta-}{EtO}\cdots H\cdots \underset{COOEt}{CMe_2}\cdots D\cdots \overset{\delta-}{OEt} \longrightarrow EtOH \; \underset{COOEt}{CMe_2}\text{—}D \; \bar{O}Et$$

The same applies to the ethoxide-catalysed racemization of optically active dialkylacetic esters.

Elimination reactions

Olefines are so frequently formed to a greater or less extent during replacement actions that it is reasonable to suppose that both processes have similar mechanisms. That this is so has been confirmed by Ingold and his school† in a most comprehensive manner.

In replacement reactions the removal of the anionoid group leaves a carbonium ion which reacts either simultaneously (S_2) or subsequently (S_1) with the anionoid reagent to form the replacement product. A second mode of stabilization of the carbonium ion is possible, however; the anionoid reagent may remove a neighbouring proton to form a C=C double bond. This process may be either simultaneous with (S_2 elimination) or subsequent to (S_1 elimination) the formation of the carbonium ion.



$$(S_2)\quad B\; H\text{—}C\text{—}C\text{—}X \rightarrow \overset{\delta+}{B}\cdots H\cdots C\cdots C\cdots \overset{\delta+}{X} \rightarrow BH^+ \; C\text{=}C \; X^-$$

$$(S_1)\quad H\text{—}C\text{—}C\text{—}X \rightarrow H\text{—}C\text{—}C^+ \; X^-$$

$$B\; H\text{—}C\text{—}C^+ \rightarrow BH^+ \; C\text{=}C$$

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† For a summary and references see Hughes and Ingold, *Trans. Faraday Soc.* **1941, 37, 657.**

The S_2 reactions will be bimolecular, the rates depending on the nature and concentrations of base, while the S_1 reaction rates should be independent of the base and its concentration. A detailed kinetic study shows that elimination reactions can indeed be divided into S_1 and S_2 types.

Both elimination reactions occur as alternatives to replacement:

$$\text{H—C—C—X} + \text{B} \begin{array}{l} \nearrow \text{H—C—C—B} \quad X^- \\ \searrow BH^+ \ \text{C=C} \quad X^- \end{array}$$

Since the rates of both S_2 elimination and replacement are given by (constant) × [H—C—C—X] × [B], their ratio must be independent of the concentration of both reagent and substrate. Similar considerations show that the relative rates of the secondary reactions of the ion (H—C—C^+) with base to give replacement or elimination products in the S_1 reaction are also constant. These predictions have been confirmed.

Moreover, in the reactions of halides (H—C—C—X) with bases (Y^-) the S_2 reaction gives more olefine than the S_1 reaction. The transition states are:

	Replacement	*Elimination*
S_2	$\text{H—C—}\underset{\underset{\overset{}{Y}^{\;\delta-}}{\vdots}}{\overset{\overset{\overset{\delta-}{X}}{\vdots}}{C}}$	$\overset{\delta-}{Y}\cdots H\cdots C\overset{\cdots}{—}C\cdots\overset{\delta-}{X}$
S_1	$\text{H—C—}\overset{\delta+}{C}\cdots\overset{\delta-}{Y}$	$\overset{\delta-}{Y}\cdots H\cdots C\overset{\cdots}{—}\overset{\delta+}{C}$

In the transition states for replacement, the charged centres are closer together; in the S_2 states the charges are like, in the S_1 opposite, and so charge interaction favours S_2 elimination and S_1 replacement. It is also clear that in the S_2 states the charge is more dispersed in the one leading to elimination; therefore an increase in dielectric constant of the solvent should favour replacement. All these conclusions have been confirmed quantitatively. The effect of changing the solvent on the relative rates of the S_1 reactions is less easily interpreted; we would expect an increase in dielectric constant to favour elimination, where the unlike charges are more separated in the transition state, but actually the opposite is true. Hughes and Ingold argue that the charges are more dispersed in the elimination transition state and therefore that increase in the dielectric constant of the solvent should favour replacement, but this argument is unsound since the charges being 'dispersed' are in fact of opposite sign. The process involves charge separation and not charge dispersal.

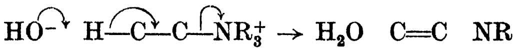
Variation in the anionoid reactivity of the reagent has a well-marked and predictable effect on the ratio of elimination to replacement. A strongly basic (anionoid) reagent has a greater affinity for hydrogen relative to carbon than a weakly basic one,† the criterion of a strong base being that it should have a great tendency to combine with H^+. Therefore a strong base will tend to attack hydrogen (elimination) rather than carbon (replacement). Conversely a weak base will favour replacement.

All these conclusions have been confirmed experimentally (see Hughes and Ingold, p. 110, for further details and references). In particular, certain apparent anomalies can be easily explained. Thus *iso*-propyl bromide gives less olefine than *tert*-butyl bromide when treated with dilute or strong solutions of sodium ethoxide in alcohol, but more olefine with intermediate concentrations. *Tert*-butyl bromide gives more olefine than *iso*-propyl bromide in both S_1 and S_2 reactions (*vide infra*); in dilute alkali both reactions are S_1, in strong alkali S_2, but at intermediate concentrations $Pr_\beta Br$ reacts mainly S_2, $Bu_\gamma Br$ mainly S_1. Since the bimolecular reaction favours elimination, $Pr_\beta Br$ under these conditions gives more olefine than $Bu_\gamma Br$. With weakly basic reagents (AcO^-, PhO^-), where the S_2 reaction no longer favours elimination strongly, $Bu_\gamma Br$ gives more olefine than $Pr_\beta Br$ at all reagent concentrations.

These results show clearly the theoretical basis of procedures that organic chemists have devised for hydrolysing halides or converting them to olefines. The former reaction, a replacement, is favoured by using weakly basic reagents in a medium of high dielectric constant; usually acetate or formate ion in water or aqueous alcohol is chosen, the resulting ester being hydrolysed subsequently to the alcohol. Preparation of the olefine, an elimination, occurs most readily with strong bases in weakly ionizing solvents; potash in absolute alcohol is the traditional choice.

Effect of structure

The structural features that decide whether a given compound undergoes S_1 or S_2 elimination are of course identical with those determining the order of the corresponding replacements, but in eliminations there are two other effects of structure to consider; the ratio of elimination to replacement, and the direction in which elimination occurs in cases where two or more different olefines may theoretically be formed. The latter problem is somewhat complex since the experimental data lead to two contradictory generalizations. Hofmann found that the elimination reactions of quaternary ammonium hydroxides,



$$HO^- \quad H{-}C{-}C{-}NR_3^+ \rightarrow H_2O \quad C{=}C \quad NR_3,$$

where any of the four groups attached to nitrogen may be eliminated, invariably gave the least substituted ethylene derivative; but Saytzeff observed that in the elimination reactions of secondary or tertiary alkyl halides with alkali, the most substituted ethylene was formed. These remarks apply to compounds where the substituents are alkyls; the effect of other substituents has been little investigated.

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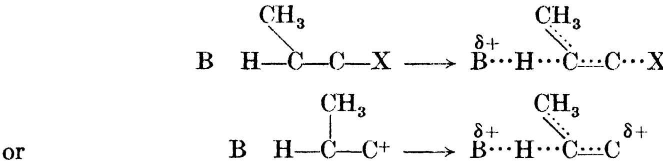
† For example, I^-, a much weaker base than OH^-, reacts more rapidly than OH^- with alkyl bromides. The reason for this difference is not known.

An alkyl substituent β to the group X which is to be eliminated will have two opposing effects. Firstly, by its —I effect it will reduce the acidity of a hydrogen attached to the β-carbon, and so lower the rate of elimination; secondly, by its —E effect it will hyperconjugate with the nascent double bond in the transition state for elimination, and so facilitate elimination.



$$\mathrm{B}\quad \mathrm{H{-}\overset{CH_3}{C}{-}C{-}X} \longrightarrow \overset{\delta+}{\mathrm{B}}\cdots\mathrm{H}\cdots\overset{CH_3}{\mathrm{C}}\overset{\cdots}{-}\mathrm{C}\cdots\mathrm{X}^{\delta-}$$

or

$$\mathrm{B}\quad \mathrm{H{-}\overset{CH_3}{C}{-}C^{+}} \longrightarrow \overset{\delta+}{\mathrm{B}}\cdots\mathrm{H}\cdots\overset{CH_3}{\mathrm{C}}\overset{\cdots}{-}\mathrm{C}^{\delta+}$$

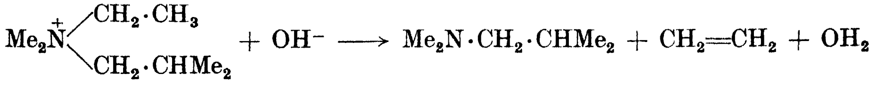
If the former effect predominates, β-alkyl substituents will reduce the rate of elimination; if the latter, they will increase it. In the α-position the I-effect of alkyl will be less, but the E-effect will be equally effective. Therefore α-substituents have little effect on reactions following Hofmann's law, where alkyl groups reduce the rate of elimination, but in Saytzeff-type reactions they increase the reaction rate almost as much as do β-substituents.

There are no good theoretical grounds for predicting which effect of alkyl will predominate in any given case. The experimental evidence shows clearly that the E-effect is more important in all S_1 eliminations, and these therefore follow Saytzeff's law. In S_2 eliminations Hofmann's rule applies in cases where the eliminated group is strongly positive in the parent compound (either an 'onium ion or a sulphonyl group); in other cases (halides) Saytzeff's law applies.

The only other substituent effect which is well established is that of E-active substituents which increase the rate of elimination, particularly in the β-position. Such groups conjugate with the incipient double bond in the transition state.

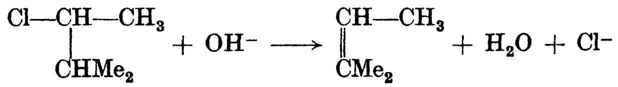
Some examples may be given to illustrate these conclusions.

1. The S_2 elimination reaction



$$\mathrm{Me_2\overset{+}{N}}\left\langle\begin{matrix}\mathrm{CH_2\cdot CH_3}\\ \mathrm{CH_2\cdot CHMe_2}\end{matrix}\right. + \mathrm{OH^-} \longrightarrow \mathrm{Me_2N\cdot CH_2\cdot CHMe_2 + CH_2{=}CH_2 + OH_2}$$

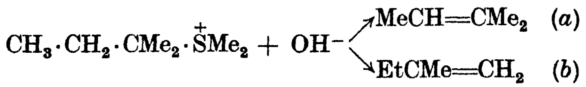
gives preferentially the less substituted ethylene; but the corresponding S_2 halide elimination



$$\begin{matrix}\mathrm{Cl{-}CH{-}CH_3}\\ |\\ \mathrm{CHMe_2}\end{matrix} + \mathrm{OH^-} \longrightarrow \begin{matrix}\mathrm{CH{-}CH_3}\\ \|\\ \mathrm{CMe_2}\end{matrix} + \mathrm{H_2O + Cl^-}$$

gives almost exclusively the more substituted ethylene.

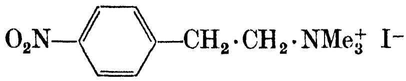
2. The elimination reaction



$$\mathrm{CH_3\cdot CH_2\cdot CMe_2\cdot\overset{+}{S}Me_2 + OH^-}\left\langle\begin{matrix}\nearrow \mathrm{MeCH{=}CMe_2}\quad (a)\\ \searrow \mathrm{EtCMe{=}CH_2}\quad (b)\end{matrix}\right.$$

gives 14 per cent. of (a) and 86 per cent. of (b) under conditions where it is bimolecular (high alkali), following Hofmann's rule; but under S_1 conditions (low alkali) the proportions are almost exactly reversed, as Saytzeff's rule requires.

3. The 'onium salt



containing a powerful +E substituent in the *β*-position, eliminates so readily that *p*-nitrostyrene is formed on adding alkali to its cold aqueous solution.

4. 1:1:2-trichloroethane with alkali gives *as*-dichloroethylene:

$$Cl_2CH{-}CH_2Cl + OH^- \rightarrow CCl_2{=}CH_2, \quad \text{not} \quad CHCl{=}CHCl.$$

The transition states for both possible eliminations are stabilized by the E-effect of two chlorine atoms, and so the decisive factor is the acidity of the eliminated hydrogen. The hydrogen whose acidity is increased by *two* neighbouring +I chlorines is eliminated.

5. The acid-catalysed dehydration of alcohols to olefines is known to follow Saytzeff's rule.† The reaction must be of S_1 type, since the intermediate is undoubtedly an oxonium ion, S_2 elimination of which would be a Hofmann-type reaction. In many cases, however, dehydration with P_2O_5 gives Hofmann-type orientation; presumably by S_2 elimination of a highly polar phosphoric ester intermediate.

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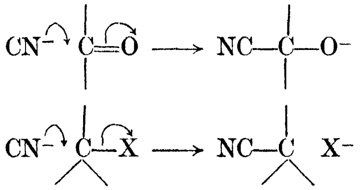
† Whitmore et al., *J.A.C.S.* 1933, **55**, 812, 1106, 1528, 3721, 5056.

CHAPTER VII

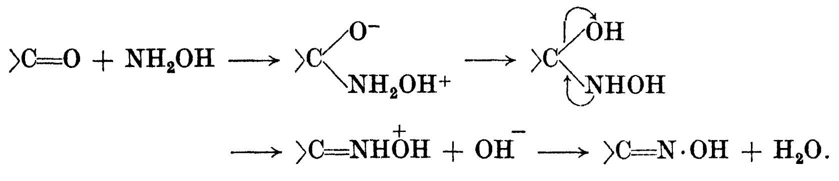
REACTIONS OF THE CARBONYL-ADDITION TYPE

REPLACEMENT reactions are not confined to compounds containing σ-bonds. A π-bond can also take part in such reactions. However, since such a bond forms only part of a multiple bond, the 'replaced group' then remains attached to the molecule by a bond of lower order. As in the case of the simple σ-replacement, such (anionoid) reactions take place most readily if the 'replaced atom' has a higher electron affinity than carbon; that is, reactivity is most marked in compounds containing such bonds as C=O, C=N, C≡N. In this chapter we shall discuss only the reactions of carbonyl compounds, since those of nitrogen-compounds (e.g. the Thorpe reaction) have been little investigated and do not differ at all in principle.

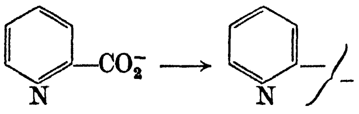
Lapworth first showed that addition reactions of aldehydes and ketones involve attack by anionoid reagents. The formation of cyanhydrin from a carbonyl compound requires basic catalysis and so the active agent must be the cyanide ion. The reaction is completely analogous to a replacement of halogen by cyanide in an alkyl halide:



The other standard reactions of aldehydes and ketones are analogous, involving attack by anions (CN^-, HSO_3^-) or anionoid reagents (NH_2OH, $Ph{\cdot}NH{\cdot}NH_2$). In the latter case the initial addition is followed by an elimination of water to give the final product.



An amusing reaction of this kind has been discovered by Hammick;† the decarboxylation of α-picolinic acid gives a pyridyl anion (cf. p. 108):



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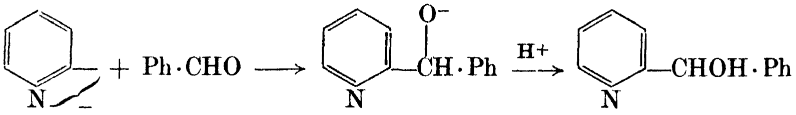
† Dyson and Hammick, *J.C.S.* 1937, 1724; Ashworth, Daffern, and Hammick, ibid. 1939, 809.

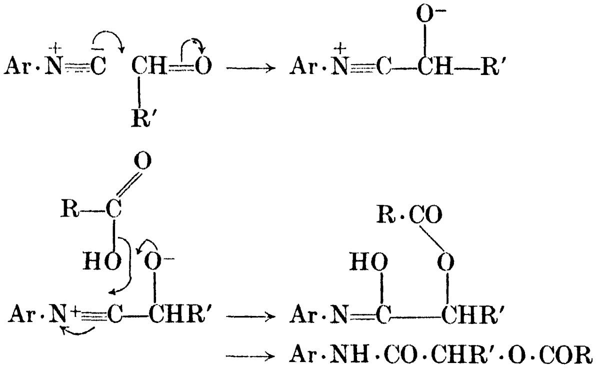
If the decarboxylation is carried out in presence of benzaldehyde, this anion adds to the carbonyl group:



The Passerini reaction is also analogous:

$$\text{R}\cdot\text{COOH} + \text{R}'\text{CHO} + \text{Ar}\cdot\overset{+}{\text{N}}{\equiv}\text{C}^- \longrightarrow \text{R}\cdot\text{CO}\cdot\text{O}\cdot\text{CHR}'\cdot\text{CO}\cdot\text{NHAr}.$$

Here the *iso*-nitrile presumably acts as an anionoid reagent, the carbon of the $—\overset{+}{\text{N}}{\equiv}\text{C}^-$ group having a pair of unshared electrons; its adduct with the aldehyde then condenses with the acid.



Effect of substituents on rates of addition

The transition state for a carbonyl addition resembles that for a $—\text{S}_2$ replacement; it will likewise be stabilized by positive and destabilized by negative substituents.

$$\text{X}^-\ \text{C}{=}\text{O} \rightarrow \overset{\delta-}{\text{X}}\cdots\text{C}{\overset{...}{=}}\overset{\delta-}{\text{O}} \rightarrow \text{X—C—O}^-$$

$$\text{X}^-\ \text{C—Y} \rightarrow \overset{\delta-}{\text{X}}\cdots\text{C}\cdots\overset{\delta-}{\text{Y}} \rightarrow \text{X—C}\quad\text{Y}^-$$

Therefore formaldehyde reacts more rapidly than other aliphatic aldehydes since the latter contain a —I alkyl substituent; ketones with two —I substituents react still more slowly. Conversely, introduction of +I chlorine atoms into the methyl of acetaldehyde increases the reactivity.

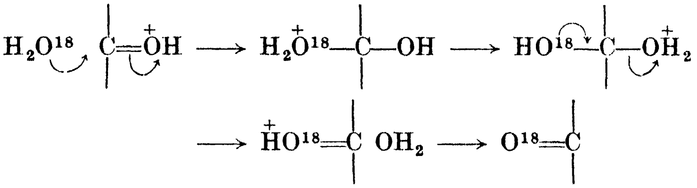
Compounds containing vinyl or phenyl groups attached to carbonyl react less readily than saturated aliphatic aldehydes. Such compounds are mesomeric, e.g.

$$\overset{\delta+}{\text{C}}{\overset{...}{=}}\text{C}{\overset{...}{=}}\overset{\delta-}{\text{O}}.$$

In the transition state for addition this mesomerism is destroyed; hence the transition state is destabilized to the extent of the resonance energy of the original carbonyl compound, and so addition is hindered.

Acid catalysis of addition

In the salts of ketones, the electron affinity of oxygen is increased, and so likewise the reactivity to anionoid reagents. Therefore such reactions are often catalysed by acids. A simple example is the acid catalysed exchange of oxygen with solvent undergone by ketones in water, which can be followed quantitatively if water enriched with the O^{18} isotope is used.† The reaction is undoubtedly



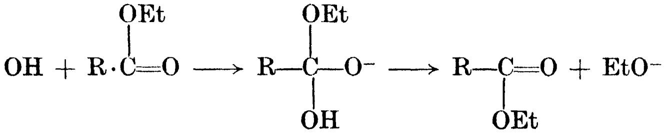
$$H_2O^{18}\ \ \overset{|}{\underset{|}{C}}=\overset{+}{O}H \longrightarrow H_2\overset{+}{O}{}^{18}-\overset{|}{\underset{|}{C}}-OH \longrightarrow HO^{18}-\overset{|}{\underset{|}{C}}-\overset{+}{O}H_2$$

$$\longrightarrow \overset{+}{H}O^{18}=\overset{|}{\underset{|}{C}}\ \ OH_2 \longrightarrow O^{18}=\overset{|}{\underset{|}{C}}$$

Another example is the formation of semicarbazones from carbonyl compounds and semicarbazide.‡

Alkaline hydrolysis of carboxylic esters

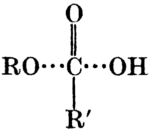
The hydrolysis of esters by alkali was formerly thought to take place by a carbonyl addition:



$$OH + R\cdot\overset{\displaystyle OEt}{\overset{|}{C}}=O \longrightarrow R-\overset{\displaystyle OEt}{\overset{|}{\underset{\displaystyle OH}{\underset{|}{C}}}}-O^- \longrightarrow R-\underset{\displaystyle OEt}{\underset{|}{C}}=O + EtO^-$$

(I)

It is now clear that this mechanism is highly improbable since the intermediate (I) is not conjugated and its formation would involve the loss of the whole resonance energy of the original ester (10–15 cals.). It is much more likely that the reaction is a normal S_2 replacement. Ethers do not react with alkali, but in the transition state for ester hydrolysis an unusual type of mesomeric stabilization will be possible. Let us consider the transition state,



$$RO\cdots\overset{\displaystyle O}{\overset{\|}{\underset{\displaystyle R'}{\underset{|}{C}}}}\cdots OH$$

Of the orbitals of the central carbon, one $2p$-orbital will be used to link the alkoxyl and hydroxyl groups; another will form part of the $C{=}O$ π-orbital; while the $R'{-}C$ and $C{-}O$ σ-bonds will be formed from the $2s$ and remaining $2p$-orbital. A little consideration shows that the transition state must be planar. The $2p$-orbitals of the alkoxyl and hydroxyl groups will then be able to overlap with the $C{=}O$ π-orbital to form a mesomeric system. Therefore in the transition state the alkoxyl and hydroxyl groups are linked by partial *double* bonds to the central carbon, not by partial *single* bonds as in a normal replacement. The transition state is therefore more stable and reaction occurs more readily than in analogous replacements of alkyl derivatives.

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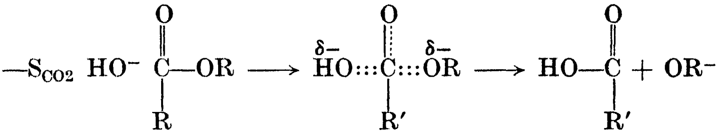
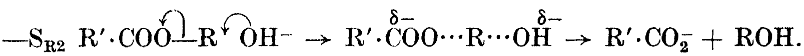
† Cohn and Urey, *J.A.C.S.* 1938, **60**, 679.

‡ Conant and Bartlett, ibid. 1932, **54**, 2881; Westheimer, ibid. 1934, **56**, 1962.



$$-S_{CO2}\ HO^- \ \underset{R}{\overset{O}{\overset{\|}{\underset{|}{C}}}}-OR \longrightarrow \overset{\delta-}{HO}\!:::\!\underset{R'}{\overset{O}{\overset{\vdots}{\underset{|}{C}}}}\!:::\!\overset{\delta-}{OR} \longrightarrow HO-\underset{R'}{\overset{O}{\overset{\|}{\underset{|}{C}}}} + OR^-$$

Another mechanism of hydrolysis is theoretically possible, a normal S_2 replacement of the acyloxy group:



$$-S_{R2}\ R'{\cdot}COO-R\ OH^- \rightarrow R'{\cdot}\overset{\delta-}{C}OO\cdots R\cdots \overset{\delta-}{OH} \rightarrow R'{\cdot}CO_2^- + ROH.$$

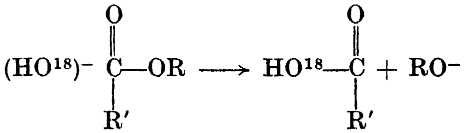
We may distinguish the mechanisms as $-S_{CO2}$ and $-S_{R2}$ respectively. Both mechanisms have unimolecular counterparts:

$$-S_{CO1}\begin{cases} R'{\cdot}CO{\cdot}OR \rightarrow R'{\cdot}\overset{+}{C}O + \overset{-}{O}R \\ R'{\cdot}\overset{+}{C}O + \overset{-}{O}H \rightarrow R'{\cdot}COOH \end{cases}$$

$$-S_{R1}\begin{cases} R'{\cdot}COOR \rightarrow R'{\cdot}CO_2^- + R^+ \\ R^+ + OH^- \rightarrow R-OH. \end{cases}$$

For reasons given above, the bimolecular reaction $-S_{R2}$ should proceed less readily than $-S_{CO2}$. The $-S_{CO1}$ reaction is also improbable on energetic grounds since in forming the intermediate $R'{\cdot}CO^+$ ion the whole of the resonance energy of the original ester would be lost.

The mechanism of normal ester hydrolysis is shown conclusively by two lines of evidence. Firstly, the reaction is bimolecular, its rate being given by $k[OH^-][\text{ester}]$, and so must be of S_2 type. Secondly, Polanyi and Szabo† have shown that if the hydrolysis is carried out in water enriched in O^{18}, none of the added isotope is found in the alcohol formed.



$$(HO^{18})^- \ \underset{R'}{\overset{O}{\overset{\|}{\underset{|}{C}}}}-OR \longrightarrow HO^{18}-\underset{R'}{\overset{O}{\overset{\|}{\underset{|}{C}}}} + RO^-$$

The $-S_{R2}$ mechanism would give alcohol containing O^{18}:

$$(HO^{18})^- + RO_2C{\cdot}R' \longrightarrow HO^{18}R + \bar{O}_2C{\cdot}R'.$$

Therefore the mechanism is indeed $-S_{CO2}$. This result is in agreement with the facts that esters of optically active alcohols give optically pure uninverted alcohols on hydrolysis (hence the mechanism must be $-S_{CO2}$ or

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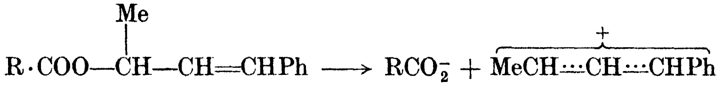
† *Trans. Faraday Soc.* **1934, 30, 508.**

$-S_{CO1}$) and that neopentyl esters hydrolyse normally† (thus excluding the S_R mechanisms: cf. p. 76).

The $-S_{R1}$ mechanism is, however, theoretically possible and has definitely been observed in certain cases. Kenyon and his collaborators‡ have shown that in the hydrolysis of esters of optically active allyl alcohols with dilute alkali racemization occurs. These conditions are peculiarly favourable for $-S_{R1}$ hydrolysis; low alkali concentration and the formation of a mesomeric allyl cation:

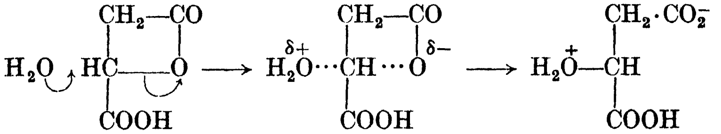


$$R\cdot COO\text{—}\overset{\overset{\displaystyle Me}{|}}{C}H\text{—}CH{=}CHPh \longrightarrow RCO_2^- + \overset{+}{\overline{MeCH{\cdots}CH{\cdots}CHPh}}$$

Moreover, the reactions give mixtures of the alcohol corresponding to the ester and its anionotropic tautomer, confirming that the allyl cation is an intermediate. In strong alkali the hydrolysis of these esters is normal, giving active alcohol by $-S_{CO2}$. Another similar reaction is the methanolysis of *tert*-butyl benzoate,§ which must involve an S_{R1} mechanism.

$$Ph_3C\text{—}O_2C\cdot Ph \rightarrow Ph_3C^+ + {}^-O_2C\cdot Ph$$
$$Ph_3C^+ + MeOH \rightarrow Ph_3C\cdot OMe$$

The only definite examples of the $-S_{R2}$ mechanism known are the hydrolyses of β-lactones in neutral solution. In $-S_{CO2}$ hydrolysis the RO group is removed intact so that esters of active alcohols should hydrolyse with retention of configuration. At neutrality, hydrolysis of optically active β-malolactone gives inverted maleic acid;‖ the reaction must be of $-S_{R2}$ type, inversion occurring since it is a normal S_2 replacement.



Effect of structure on rate of hydrolysis

The $-S_{CO2}$ hydrolysis of esters is a special kind of $-S_2$ replacement and its rate will be similarly affected by substituents. That is, positive substituents will increase, negative decrease the rate. Moreover, the hydrolysis of esters of trialkylacetic acids is abnormally difficult for the same reason that neopentyl halides are unreactive (p. 76); the hydroxyl ion is hindered from adopting its preferred line of approach (along the axis of the C—O alkyl bond). It is quite likely that many such esters hydrolyse by the unhindered $-S_{R2}$ mechanism and a study of the reaction from this point of view would be interesting.

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† Quayle and Norton, *J.A.C.S.* 1940, **62**, 1170.

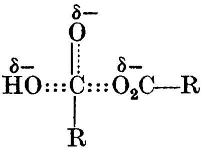
‡ Kenyon, Partridge, and Phillips, *J.C.S.* 1936, 85; Hills, Kenyon, and Phillips, ibid., p. 576.

§ Cohen and Schneider, *J.A.C.S.* 1941, **63**, 3382.

‖ Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.C.S.* 1937, 1264.

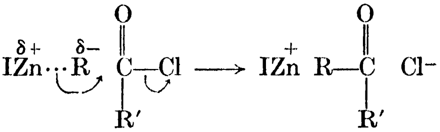
Other reactions of carboxylic acid derivatives

The hydrolysis of amides, acid chlorides, and anhydrides by alkali are precisely analogous to the ester hydrolysis and presumably take place by the $-S_{CO2}$ mechanism. Acid chlorides react more readily, amides less readily than esters, since the electron affinity of chlorine is greater, and of nitrogen less than that of oxygen. Anhydrides also react more readily than esters because in the transition state



$$\overset{\delta-}{HO}:::\overset{\overset{\delta-}{O}}{\overset{\|}{\underset{\underset{R}{|}}{C}}}:::\overset{\delta-}{O_2}C{-}R$$

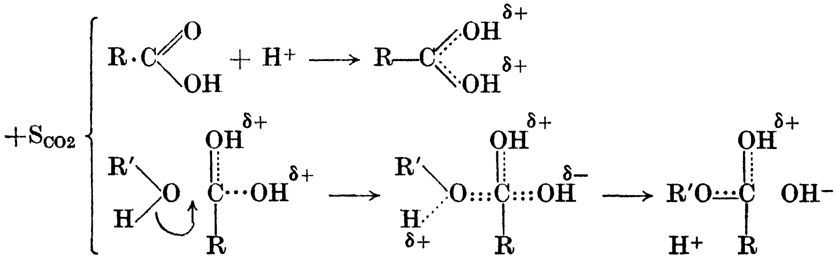
the oxygen being eliminated can conjugate with the second acyl group. Other reactions of acid derivatives with anionoid reagents, for example the conversion of esters to amides with ammonia, or of acid chlorides to ketones by alkyl zinc iodides (Blaise reaction), also formally resemble ester hydrolysis.



$$\overset{\delta+}{IZn}\cdots\overset{\delta-}{R}\ \overset{O}{\overset{\|}{\underset{\underset{R'}{|}}{C}}}{-}Cl \longrightarrow \overset{+}{IZn}\ R{-}\overset{O}{\overset{\|}{\underset{\underset{R'}{|}}{C}}}\ Cl^-$$

Acid-catalysed reactions of carboxyl derivatives

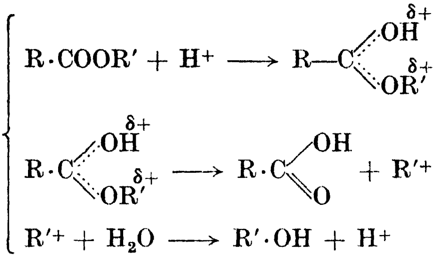
The hydrolysis of esters and the reverse reaction—the formation of esters from acids—can be catalysed by acids. The most obvious mechanism for these reactions would be a primary addition of a proton to the acid to give a highly reactive salt (cf. acid-catalysed carbonyl reactions, p. 117). The salt could then undergo a $-S_{CO2}$ replacement with undissociated water or alcohol.


+S_CO2
R·C O OH + H+ → R—C OH δ+ OH δ+
R′ O H, OH δ+ C···OH δ+ R → R′ O:::C:::OH δ− H δ+ R → R′O—C OH δ+ OH− H+ R

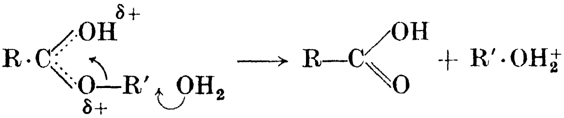
Since this reaction is so similar to the $-S_{CO2}$ hydrolysis, it is reasonable to suppose that acid-catalysed counterparts might be found to the other modes of alkaline hydrolysis. The theoretically possible reactions are:

$$+S_{CO1}\begin{cases} R\cdot CO\cdot OR' + H^+ \longrightarrow R\cdot \overset{+}{CO} + HOR' \\ R\cdot CO^+ + H_2O \longrightarrow R\cdot COOH + H^+ \end{cases}$$

$+S_{R1}$

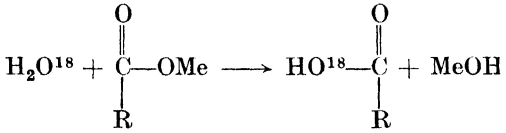


$+S_{R2}$

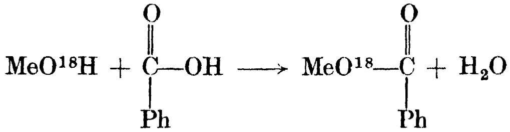


In each case esterification might occur by an analogous reaction between the acid and alcohol. Esterification, or hydrolysis of esters of optically active alcohols, by $+S_{CO}$ mechanisms, should take place without change of configuration or racemization; by $+S_{R1}$ with partial or complete racemization; and by $+S_{R2}$ with complete inversion.

Experiments with the heavy oxygen isotope show that the $+S_{CO2}$ mechanism is the normal one. The acid-catalysed hydrolysis of methyl hydrogen succinate in water enriched with O^{18} gives methanol free from excess of O^{18},[†] while the esterification of benzoic acid in methanol containing excess O^{18} gives normal water.[‡]



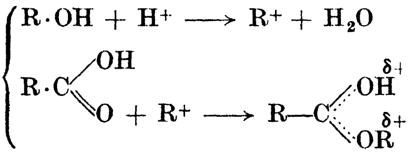
$$H_2O^{18} + R\text{—}C(=O)\text{—}OMe \longrightarrow HO^{18}\text{—}C(=O)\text{—}R + MeOH$$



$$MeO^{18}H + Ph\text{—}C(=O)\text{—}OH \longrightarrow MeO^{18}\text{—}C(=O)\text{—}Ph + H_2O$$

Moreover, acid-catalysed esterification of alcohols is generally bimolecular and as a rule optically active alcohols give active esters; although the racemization[§] of 2-octanol during esterification with sulphuric-acetic acids may indicate that the $+S_{R1}$ mechanism is operating in this case:

$+S_{R1}$



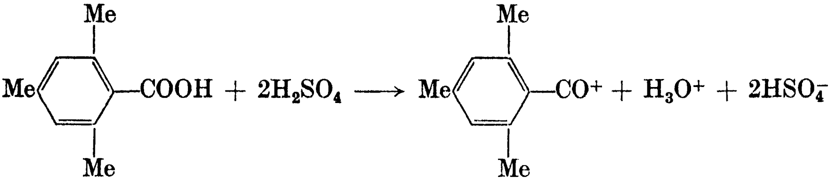
The details of these mechanisms need not be discussed since they will be obvious from analogy with what has gone before, but it may be noted that the free protons, written for convenience in the equations, are in actual fact solvated, forming oxonium ions with the water or alcohol present.

[†] Datta, Day, and Ingold, *J.C.S.* 1939, 838.

[‡] Roberts and Urey, *J.A.C.S.* 1938, **60**, 2391; 1939, **61**, 2584.

[§] Hughes, Ingold, and Masterman, *J.C.S.* 1939, 840.

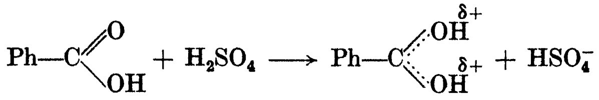
No evidence for the $+S_{R2}$ mechanism has been reported, but a few special cases are known where reaction takes place by mechanism $+S_{CO1}$. Hydrolysis of esters of mesitylenic acid is usually difficult, since the carbalkoxyl group is sterically hindered; but if such an ester is dissolved in cold concentrated sulphuric acid and the solution poured into water, mesitylenic acid is formed quantitatively and instantly.[†] Conversely, pouring a solution of the acid in sulphuric acid into alcohol gives a theoretical yield of ester. Now Treffers and Hammett[‡] have shown that mesitylenic acid and its esters give four-fold depression of freezing-point in concentrated sulphuric acid solution, where each molecule of acid or ester must therefore give four ions. The only reasonable explanation of this result is that trimethylbenzoyl cations are formed:



On pouring the solution into water or alcohol, this cation reacts at once with the solvent:

$$C_9H_{11}\cdot CO^+ + ROH \rightarrow C_9H_{11}\cdot COOR + H^+.$$

Reactions of this type seem to occur only with sterically hindered aromatic acids. Normally the $+S_{CO1}$ mechanism should be energetically most unfavourable, since it requires the destruction of a conjugated system. In the case of benzoic acids the resulting acyl is mesomeric and stabilized and this facilitates reaction. However, benzoic acids are themselves mesomeric, the benzene ring and carboxyl group being conjugated, and so the $+S_{CO1}$ reaction is still unfavourable; such acids give only a two-fold depression of freezing-point in H_2SO_4.



$$Ph\text{—}C\begin{matrix}\nearrow O\\ \searrow OH\end{matrix} + H_2SO_4 \longrightarrow Ph\text{—}C\begin{matrix}\nearrow \overset{\delta+}{OH}\\ \searrow OH^{\delta+}\end{matrix} + HSO_4^-$$

But in sterically hindered benzoic acids the carboxyl is prevented from adopting the configuration coplanar with the ring which is essential for conjugation (cf. p. 200); therefore they present the most favourable possible case for the $+S_{CO1}$ reaction. (The benzoyl cation, $Ph\cdot\overset{+}{CO}$, is probably linear and so *ortho* substituents will not affect its stability.)

[†] Newman, *J.A.C.S.* 1941, **63**, 2431.
[‡] Ibid. 1937, **59**, 1708.

Hydrolysis of sulphuric esters

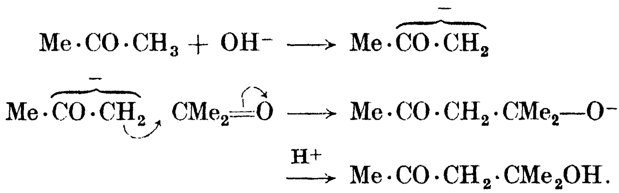
Experiments with O^{18} have shown that sulphonic esters invariably hydrolyse with C—O and not S—O bond-fission:

$$H\overset{-}{O}{}^{18} + ROSO_2R' \rightarrow HO^{18}R + {}^{-}O_3SR'$$

The sulphonate group therefore behaves in exactly the same way as a halogen atom in a simple replacement, the reaction thus presenting no new features.

The aldol condensation

A series of special cases of carbonyl and carboxyl reactions are known in which the anionoid reagent is a mesomeric anion. The aldol condensation of carbonyl compounds by bases is the simplest example; part of the carbonyl compound is converted into its conjugate anion by the base and the anion then adds to the carbonyl group of another molecule of reactant. Acetone, for example, gives diacetone alcohol with alkali:



$$\mathrm{Me\cdot CO\cdot CH_3} + \mathrm{OH^-} \longrightarrow \mathrm{Me\cdot}\overset{-}{\overbrace{\mathrm{CO\cdot CH_2}}}$$

$$\mathrm{Me\cdot}\overset{-}{\overbrace{\mathrm{CO\cdot CH_2}}},\ \mathrm{CMe_2{=}O} \longrightarrow \mathrm{Me\cdot CO\cdot CH_2\cdot CMe_2{-}O^-} \xrightarrow{H^+} \mathrm{Me\cdot CO\cdot CH_2\cdot CMe_2OH}.$$

The most definite evidence for this mechanism is the fact that the aldol condensation of acetaldehyde is bimolecular† and not termolecular, the rate being given approximately by $k[CH_3\cdot CHO][OH']$. The rate-determining step must be a reaction of aldehyde with hydroxyl ion to form a reactive intermediate which condenses rapidly with a second aldehyde molecule. The intermediate can only be the anion $(CH_2\overset{..}{=}CHO)^-$. The aldol condensation is therefore a special type of prototropic reaction. From the equations on p. 22 it is clear that aldol formation, which may be represented:

$$\mathrm{R\cdot CO\cdot CR_2H} + \mathrm{OH'} \rightarrow \mathrm{R\cdot CO\cdot CR_2^-} + \mathrm{H_2O} \quad \text{(i)}$$

$$\mathrm{R\cdot CO\cdot CR_2^-} + \mathrm{H_2O} \rightarrow \mathrm{R\cdot CO\cdot CR_2H} + \mathrm{OH^-} \quad \text{(ii)}$$

$$\mathrm{R\cdot CO\cdot CR_2^-} + \mathrm{R\cdot CO\cdot CR_2H}\ (+\ \mathrm{H^+}) \rightarrow \mathrm{R\cdot CO\cdot CR_2\cdot CROH\cdot CR_2H} \quad \text{(iii)}$$

should proceed at a rate given by

$$\frac{k_1 k_3 [\mathrm{OH'}][\mathrm{R\cdot CO\cdot CR_2H}]^2}{k_2 + k_3 [\mathrm{R\cdot CO\cdot CR_2H}]}. \quad (1)$$

If the rate of condensation of the intermediate enolate ion with carbonyl compound is large, the overall rate approximates to that of the first step and is of first order with respect to the carbonyl compound. The rate of reaction is equal to the rate of ionization. Acetaldehyde exemplifies this

† Bell, *J.C.S.* 1937, 1637.

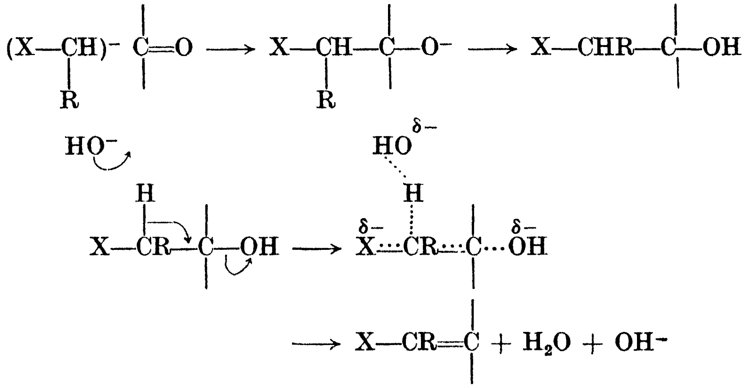
limiting case. If, on the other hand, condensation is slow, condensation becomes rate-determining and the overall rate will be given by

$$\frac{k_1 k_3}{k_2}[\mathrm{OH'}][\mathrm{R\cdot CO\cdot R'}]^2. \tag{2}$$

Acetone follows these kinetics. It is interesting that at a given concentration of alkali the rate of aldolization of acetone is much less than the rates of base-catalysed halogenation; the overall rate of aldolization is much less than the rate at which acetone is converted into $(\mathrm{CH_3\cdot CO\cdot CH_2})^-$ by alkali.

If the rates of reactions (ii) and (iii) are comparable, the rate-expression cannot be simplified and the reaction will not be of any definite order with respect to the carbonyl compound, although over limited ranges of concentration the rate may be approximately proportional to some power of the carbonyl concentration between 1 and 2. *Iso*-butyraldehyde is a good example.†

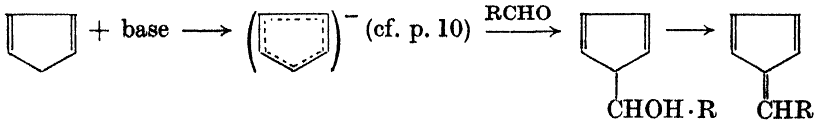
Similar reactions are given by other enolate ions with carbonyl compounds. Thus the enolate of one carbonyl compound may be condensed with the carbonyl group of another; or the enolate of a nitro-compound, nitrile, malonic ester, etc., may be employed. In many cases the aldol first formed is rapidly dehydrated by the basic catalyst to give an unsaturated compound; the dehydration takes place readily since in the transition state for dehydration (a $-\mathrm{S_2}$ elimination) the hydroxyl and the $+\mathrm{E}$ group of the enolate component are both conjugated with the nascent double bond.



Some examples of such condensations are:

$$\mathrm{PhCHO} + (\mathrm{CH_2\cdot CO\cdot CH_3})^- \rightarrow (+\,\mathrm{H^+}) \rightarrow \mathrm{Ph\cdot CHOH\cdot CH_2\cdot CO\cdot CH_3}$$
$$\rightarrow \mathrm{Ph\cdot CH{=}CH\cdot CO\cdot CH_3}$$

$$\mathrm{R\cdot CHO} + (\mathrm{CH_2\cdot NO_2})^- \rightarrow \mathrm{R\cdot CHOH\cdot CH_2\cdot NO_2} \rightarrow \mathrm{R\cdot CH{=}CH\cdot NO_2}$$



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† Neill, quoted by Bell, *Trans. Faraday Soc.* 1941, **37**, 717.

Effect of substituents on the rate of aldol condensations

When the rate of the overall reaction is determined by that of enolization, substituents will have the same effect on it that they have on prototropic reactions in general (Chapter VI). That is, negative substituents will lower the rate, positive increase it. Unfortunately no quantitative data seem to be available, but qualitatively there can be no doubt that higher aliphatic aldehydes of the type $R{\cdot}CH_2CHO$ react less readily, phenylacetaldehyde more readily than acetaldehyde.

In the majority of aldol condensations, however, the slow step is the addition of enolate ion to the carbonyl group. The rate is then given by equation (2) (p. 124), which may be written

$$-\frac{d[R_2CO]}{dt} = K_A k_3[R_2CO]^2[OH'],$$

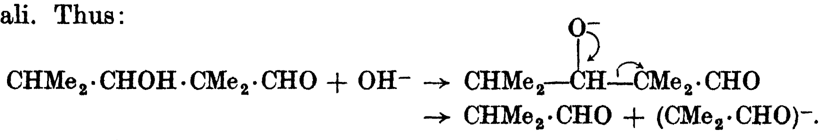
where K_A is the acid dissociation constant of R_2CO. We might suppose then that the rate would vary directly as K_A. However, the value of k_3 depends on the anionoid reactivity of the enolate ion; this will naturally be smaller, the stronger the acid from which it is formed. Therefore the greater K_A, the smaller k_3, and so substituents which merely vary K_A in the enolate component should have comparatively little effect on the overall rate of reaction; and this residual effect cannot be predicted even in qualitative terms. On the other hand, substituents in the carbonyl component will affect the reactivity of the carbonyl and hence the rate of condensation, according to the general principles laid down earlier (negative substituents decrease, positive increase the rate). Coombs and Evans† have found that in the condensation of benzaldehyde with acetophenone derivatives,

$$\begin{aligned}\mathrm{Ph{\cdot}CHO + (Ph{\cdot}CO{\cdot}CH_2)^-} &\rightarrow \mathrm{Ph{\cdot}CHOH{\cdot}CH_2{\cdot}CO{\cdot}Ph}\\ &\rightarrow \mathrm{Ph{\cdot}CH{=}CH{\cdot}CO{\cdot}Ph,}\end{aligned}$$

the activation energy of the reaction is altered little by substituents in the ketone, but markedly by substituents in the aldehyde. This agrees exactly with our predictions (Watson‡ has interpreted these results in a different and erroneous manner).

Reverse aldol reactions

The aldol condensation is reversible in cases where no subsequent complications arise (dehydration or further condensation of the aldol). The reverse reaction is an unusual type of $-S_2$ replacement where the replaced group is a carbanion stabilized by a $+E$ substituent, and it has been observed in the reactions of diacetone alcohol and *iso*-butyraldol with alkali. Thus:



$$\begin{aligned}\mathrm{CHMe_2{\cdot}CHOH{\cdot}CMe_2{\cdot}CHO + OH^-} &\rightarrow \mathrm{CHMe_2{-}\overset{O^-}{C}H{-}CMe_2{\cdot}CHO}\\ &\rightarrow \mathrm{CHMe_2{\cdot}CHO + (CMe_2{\cdot}CHO)^-.}\end{aligned}$$

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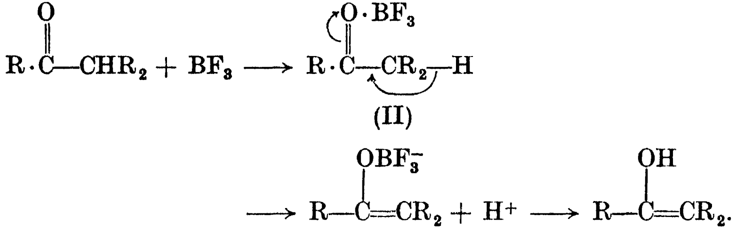
† *J.C.S.* 1940, 1295.

‡ *Trans. Faraday Soc.* 1941, **31**, 711. See Ingold, ibid., p. 718.

In these cases the action of alkali leads to an equilibrium between carbonyl compound and aldol. Substituents in the carbonyl compound which stabilize it will reduce the amount of aldol at equilibrium. Since the C=O group is +E, +I, the carbonyl compound will be stabilized by —I substituents. Thus the equilibrium in ketones is much less favourable to aldol than it is in aldehydes. This is seen clearly in the case of acetone and *iso*-butyraldehyde.

Acid-catalysed aldol condensation

Acids or 'generalized acids' such as BF_3 can catalyse aldol condensations. Very little is known about the reactions, but from analogy it seems clear that the catalyst first enolizes some of the reactant:

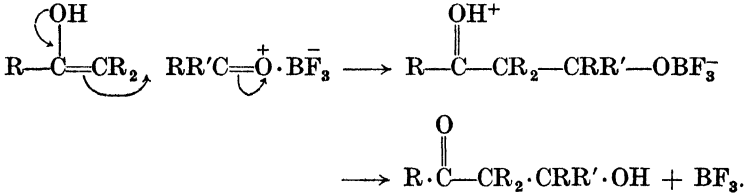


$$R\cdot\overset{\overset{\displaystyle O}{\|}}{C}—CHR_2 + BF_3 \longrightarrow R\cdot\overset{\overset{+\;\;-}{O\cdot BF_3}}{\overset{\|}{C}}—CR_2—H$$

(II)

$$\longrightarrow R—\overset{\overset{OBF_3^-}{|}}{C}=CR_2 + H^+ \longrightarrow R—\overset{\overset{OH}{|}}{C}=CR_2.$$

The enol then reacts with the oxonium salt (II):



$$R—\overset{\overset{OH}{|}}{C}=CR_2\quad RR'C=\overset{+}{O}\cdot\overset{-}{B}F_3 \longrightarrow R—\overset{\overset{OH^+}{\|}}{C}—CR_2—CRR'—OBF_3^-$$

$$\longrightarrow R\cdot\overset{\overset{O}{\|}}{C}—CR_2\cdot CRR'\cdot OH + BF_3.$$

The enol is a much weaker anionoid reagent than the corresponding enolate, but this is compensated by the much greater cationoid reactivity of the salt compared with that of the parent carbonyl compound.

The Perkin reaction

This is a special case of the aldol condensation in which the carbanion is the enolate ion from an acid anhydride. Perkin originally proposed this mechanism, but later authors were of the opinion that the acid anhydride acted merely as a condensing agent, the sodium salt used actually reacting with the aldehyde. Recently Breslow and Hauser† have shown that the same mixture of cinnamic and α-ethylcinnamic acids is formed from benzaldehyde by the action of acetic anhydride and sodium butyrate as by butyric anhydride and sodium acetate. Under the conditions of reaction an equilibrium is set up between the two anhydrides and the two sodium salts. The equilibrium varies with temperature, and the relative yields of cinnamic and ethylcinnamic acids vary in rough proportion with the equilibrium concentrations of the two anhydrides, suggesting strongly that it is the anhydride which condenses with the aldehyde. This argument is not quite conclusive since the temperature coefficients of the two reactions might differ. However, if it were the sodium salt which reacts, the $—CO_2^-$ group would be the activator for reaction and so sodium malonate should condense even more readily than sodium acetate. Actually Breslow and Hauser were unable to condense sodium malonate with benzaldehyde in the absence of acid anhydrides (which could give mixed malonic anhydrides with sodium malonate). Acetic anhydride, on the other hand, reacts readily with benzaldehyde in the absence of sodium acetate, provided some other base (pyridine, triethylamine, sodium phosphate, etc.) is present.† In any case it is difficult to see any reasonable electronic process whereby sodium acetate could condense with a carbonyl group, and so there can be little doubt that the mechanism of the Perkin reaction is

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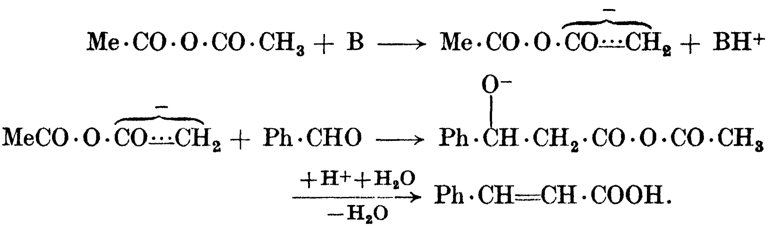
† *J.A.C.S.* 1939, **61**, 786.



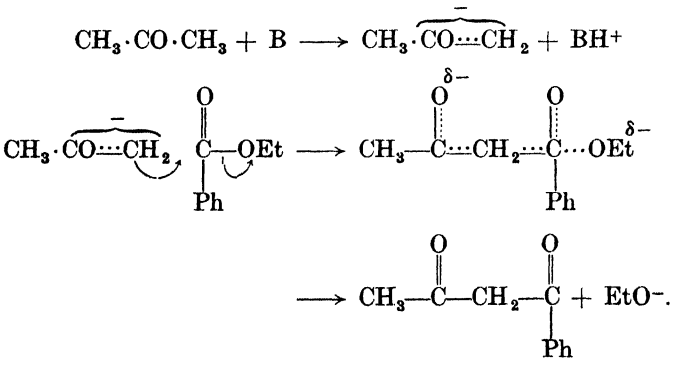
$$\mathrm{Me{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3 + B \longrightarrow Me{\cdot}CO{\cdot}O{\cdot}\overset{-}{\overgroup{CO{\cdots}CH_2}} + BH^+}$$

$$\mathrm{MeCO{\cdot}O{\cdot}\overset{-}{\overgroup{CO{\cdots}CH_2}} + Ph{\cdot}CHO \longrightarrow Ph{\cdot}\overset{\overset{O^-}{|}}{C}H{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3}$$

$$\xrightarrow[-\mathrm{H_2O}]{+\mathrm{H^+}+\mathrm{H_2O}} \mathrm{Ph{\cdot}CH{=}CH{\cdot}COOH.}$$

The Claisen condensation

Just as the aldol condensation is a special case of carbonyl addition, the reagent being a mesomeric carbanion, so is the Claisen condensation a similar variant of $-S_{CO2}$ ester replacement. One component in the reaction is converted to a carbanion by the basic catalyst, and this anion then replaces alkoxyl from the second component. Thus the condensation of ethyl benzoate with acetone may be represented:



$$\mathrm{CH_3{\cdot}CO{\cdot}CH_3 + B \longrightarrow CH_3{\cdot}\overset{-}{\overgroup{CO{\cdots}CH_2}} + BH^+}$$

$$\mathrm{CH_3{\cdot}\overset{-}{\overgroup{CO{\cdots}CH_2}}\ \underset{\underset{Ph}{|}}{\overset{\overset{O}{\|}}{C}}{-}OEt \longrightarrow CH_3{-}\overset{\overset{\delta-}{\overset{O}{\vdots}}}{C}{\cdots}CH_2{\cdots}\underset{\underset{Ph}{|}}{\overset{\overset{O}{\vdots}}{C}}{\cdots}OEt^{\delta-}}$$

$$\longrightarrow \mathrm{CH_3{-}\overset{\overset{O}{\|}}{C}{-}CH_2{-}\underset{\underset{Ph}{|}}{\overset{\overset{O}{\|}}{C}} + EtO^-.}$$

The mechanism of this reaction was long obscured by the fact that the analogous self-condensation of esters could only be effected if they had two hydrogen atoms attached to the α-carbon, when the normal condensing agents (Na, NaOEt, $NaNH_2$, etc.) were used. Hauser and Renfrow[†] have recently shown that the self-condensation of ethyl *iso*-butyrate can be brought about by the use of a more basic condensing agent ($\overset{+}{Na}\cdot CPh_3^-$). It is therefore clear that the failure of classical reagents was due to the extremely low acidity of the ester. The acidity of a C—H group is lowered by negative substituents, and hence dialkylacetic esters are less acidic than monoalkyl analogues. Esters are in any case much less acidic than ketones, since the —COOR group has a much smaller +E effect than —COR. The self-condensation of ethyl *iso*-butyrate can also be effected by other very strong bases, for example, by mesitylmagnesium bromide.[‡]

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† Kalnin, *Helv. Chim. Acta*, **1928**, **11**, **977**.

The effect of structure on the rates of Claisen condensation has been little studied quantitatively. The general principles can be easily deduced. The reactivity of the second (ester) component will be increased by positive substituents, decreased by negative substituents. The reactivity of the first (carbanion) component will be affected by substituents in the opposite way. On the other hand, the concentration of enolate present at equilibrium will be increased by positive and decreased by negative substituents. The qualitative evidence available supports these conclusions. Thus the ease of condensation with anions falls in the series

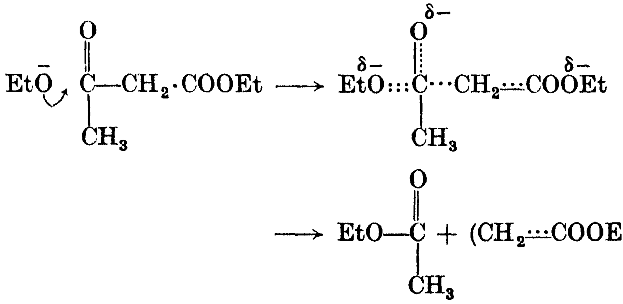
$$CH_3\cdot COOEt > CH_3\cdot CH_2\cdot COOEt > (CH_3)_2CH\cdot COOEt;$$

and also in the series

$$Me\cdot COOMe > Me\cdot COOEt > Me\cdot COOPr_\beta > Me\cdot COOBu_\gamma.$$

(*Tert*-butyl acetate actually forms a stable enolate with sodium triphenylmethyl.[§]) Acetone reacts more readily than acetylacetone with esters and sodium ethoxide, acetylacetone giving much the less reactive anion. And finally ethyl *iso*-butyrate fails to react with bases which can readily convert ethyl acetate into acetoacetic ester.

The Claisen condensation also resembles the aldol condensation in being reversible,[||] the reverse action being a simple $-S_2$ replacement,



$$\overset{-}{EtO}\ \overset{\displaystyle O}{\underset{\displaystyle CH_3}{\overset{\|}{\underset{|}{C}}}}{-}CH_2\cdot COOEt \longrightarrow \overset{\delta-}{EtO}\!:::\!\overset{\displaystyle \overset{\delta-}{O}}{\underset{\displaystyle CH_3}{\overset{\vdots\|}{\underset{|}{C}}}}\cdots CH_2\text{-\!-\!-}\overset{\delta-}{COOEt}$$

$$\longrightarrow EtO{-}\overset{\displaystyle O}{\underset{\displaystyle CH_3}{\overset{\|}{\underset{|}{C}}}} + (CH_2\text{-\!-\!-}COOEt)^-$$

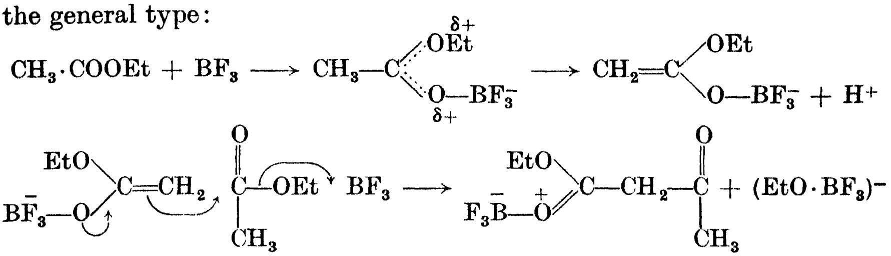
[†] *J.A.C.S.* 1937, **59**, 1823; 1938, **60**, 463.

[‡] Spielman and Schmidt, ibid. 1937, **59**, 2009.

[§] Hudson and Hauser, ibid. 1941, **63**, 3156.

[||] Beckmann and Adkins, ibid. 1934, **56**, 1119.

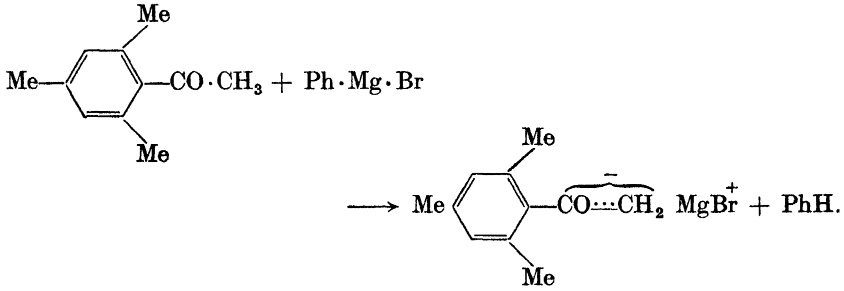
The condensation can, moreover, be brought about by 'generalized acids' such as $AlCl_3$ or BF_3; in this case normal acids either are not strong enough or react with the ester in some other way. These acid-catalysed Claisen reactions have been little investigated; presumably the mechanism is of the general type:



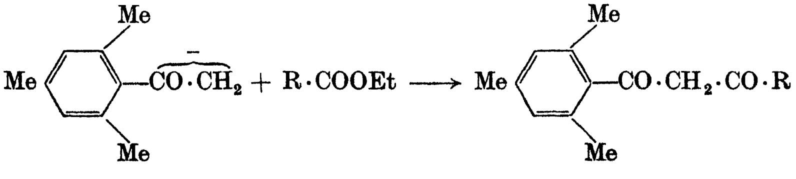
For clarity classical structures have been written for the mesomeric intermediates.

Miscellaneous reactions

The carbonyl addition reaction and the ester replacement are both formally analogous to $-S_2$ replacements. In both reactions the 'entering' and 'leaving' groups adopt, if they can, a configuration in line with the central carbon in the transition state. As in the case of neopentyl halides, this configuration may be made impossible by bulky α-substituents, and in that case the normal reaction occurs only with difficulty and unusual alternatives may be observed. Thus the Grignard reagent normally attacks the carbonyl group of ketones, but if this reaction is hindered, an alternative attack on α-hydrogen may lead to enolization instead. This effect was first observed in the case of methyl mesityl ketone which gives the enolate with phenyl magnesium bromide:†



The resulting enolate gives normal reactions since the terminal methylene is not hindered. Thus it will condense with esters to give β-diketones:



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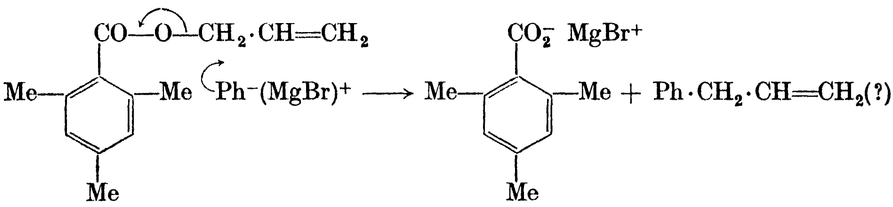
† Fuson, Fugate, and Fisher, ibid. 1939, **61**, 2362.

The effect of groups of different sizes has been investigated by Whitmore and Lewis;[†] their results (Table 19) show clearly how the amount of 'abnormal' reaction (enolization) with methyl magnesium bromide increases with the size of the substituents.

TABLE 19

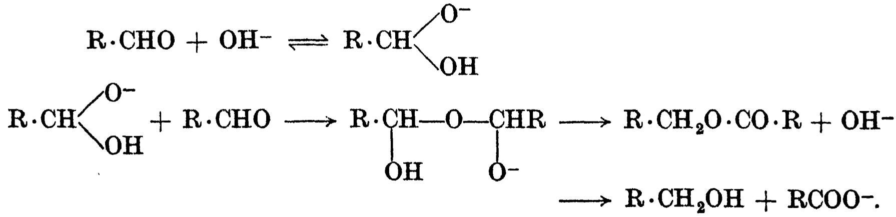
Compound	*% Enol*
$Me_3C \cdot CH_2 \cdot CO \cdot CH_3$	0
$Me_3C \cdot CO \cdot CH_3$	5
$Me_2EtC \cdot CO \cdot CH_3$	14
$MeEt_2C \cdot CO \cdot CH_3$	84
$Et_3C \cdot CO \cdot CH_3$	94

An analogous abnormal reaction of esters was reported recently by Arnold, Bank, and Liggett;[‡] allyl mesitylenate with phenyl magnesium bromide gives a salt of mesitylenic acid (and presumably allylbenzene).



The Cannizzaro reaction

This reaction, a disproportionation of aldehydes to alcohol and acid under the influence of hydroxyl ion, has been much studied. It is shown by most aldehydes that cannot undergo aldol condensation; that is, by aromatic aldehydes, tertiary aliphatic aldehydes, and formaldehyde. The reactions are of the third or fourth order, their rates being given by $k[\mathrm{RCHO}]^2[\mathrm{OH}']$ or $k[\mathrm{RCHO}]^2[\mathrm{OH}']^2$. That of furfural, for instance, is invariably of the fourth order,[§] while that of benzaldehyde is of fourth order in strong alkali, third order in weak alkali.[||] Since simple reactions of such high order are almost unknown, the Cannizzaro reaction must almost certainly take place in stages. The generally accepted mechanism is a modification of the Lapworth benzoin mechanism (*vide infra*). The aldehyde first reversibly adds hydroxyl ion. The resulting anion then adds to the second aldehyde molecule and the adduct then rearranges:



$$R \cdot CHO + OH^- \rightleftharpoons R \cdot CH\begin{matrix} O^- \\ OH \end{matrix}$$

$$R \cdot CH\begin{matrix} O^- \\ OH \end{matrix} + R \cdot CHO \longrightarrow R \cdot \underset{OH}{CH}—O—\underset{O^-}{CHR} \longrightarrow R \cdot CH_2O \cdot CO \cdot R + OH^-$$

$$\longrightarrow R \cdot CH_2OH + RCOO^-.$$

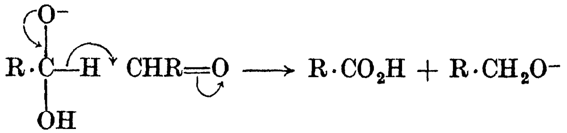
[†] *J.A.C.S.* 1942, **64**, 2964.

[‡] Ibid. p. 2875.

[§] Geib, *Z. phys. Chem.* 1934, A **169**, 41.

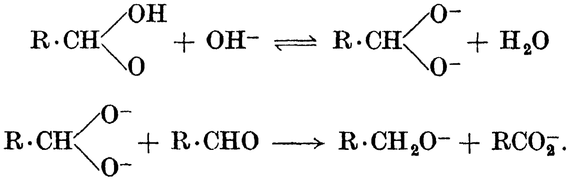
[||] Pomeranz, *Monat.* 1900, **21**, 389; Euler and Lövyrer, *Z. anorg. allgem. Chem.* 1925, **127**, 123.

An alternative possibility is a direct transfer of negative hydrogen from the initial ion to aldehyde,



$$R\cdot\overset{O^-}{\underset{OH}{C}}-H\ \ CHR{=}O \longrightarrow R\cdot CO_2H + R\cdot CH_2O^-$$

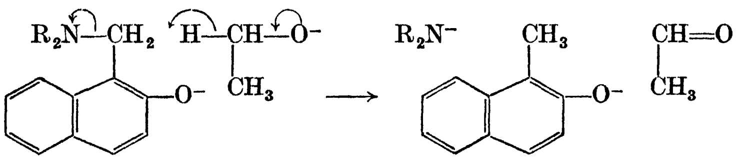
but the isolation by Lachman[†] of benzyl benzoate from the reaction between benzaldehyde and alkali under mild conditions supports the former scheme. Both lead to a third-order expression for the overall rate. Fourth-order kinetics can be explained if the first step is the reversible formation of a doubly charged anion from the aldehyde, this doubly charged ion then reacting with the second aldehyde molecule:



$$R\cdot CH\left\langle\begin{matrix}OH\\O\end{matrix}\right. + OH^- \rightleftharpoons R\cdot CH\left\langle\begin{matrix}O^-\\O^-\end{matrix}\right. + H_2O$$

$$R\cdot CH\left\langle\begin{matrix}O^-\\O^-\end{matrix}\right. + R\cdot CHO \longrightarrow R\cdot CH_2O^- + RCO_2^-.$$

This general mechanism explains well the fact that no hydrogen attached to carbon is exchanged for deuterium when the reaction is carried out in deuterium oxide solution.[‡] The reaction also falls into line with others where hydrogen is transferred as H^-, the hydrogen being activated in the donor by an adjacent —E substituent. Apart from reactions analogous to the Cannizzaro reaction, we may mention the reduction of neopentyl iodide by sodium ethoxide (p. 82), and the analogous reduction of piperidinomethyl-β-naphthol[§] by the same reagent.



The ease of the hydrogen transfer will depend mainly on the cationoid reactivity of the acceptor molecule. Changes of structure in the donor will affect the initial equilibrium of aldehyde with alkali, and the reactivity of the resulting anion, oppositely, and hence will affect the rate to a smaller and unpredictable extent (cf. the aldol condensation, p. 125). Therefore negative substituents in an aldehyde should reduce the rate of its Cannizzaro reaction since they will lower the cationoid reactivity of carbonyl; conversely, positive substituents should increase the rate. This effect is shown qualitatively by the complete failure of *o*- and *p*-hydroxy-benzaldehyde derivatives to undergo the reaction, the groups *o*- and *p*-($^{-}O \cdot C_6H_4$—) having a powerful —E effect. In *m*-hydroxy-benzaldehyde the —E activity is much smaller and so the Cannizzaro reaction does take place. Quantitatively the relationship between rate of reaction and structure is well shown in the following table of relative reaction rates of substituted benzaldehydes. The aldehydes are arranged in order of increasing —E activity of the substituted phenyl group (cf. Chapter IX).

[†] *J.A.C.S.* 1923, **45**, 2356; ref. ‡, p. 132.

[‡] Bonhoeffer and Fredenhagen, *Naturwiss.* 1937, **25**, 459.

[§] Cornforth, Cornforth, and Robinson, *J.C.S.* 1942, 682.

TABLE 20†

Compound	*Relative rate of reaction*
m-Nitrobenzaldehyde	172
m-Chlorobenzaldehyde	42
p-Chlorobenzaldehyde	14·4
Benzaldehyde	1
p-Isopropylbenzaldehyde	0·74
p-Methoxybenzaldehyde	0·45
p-Dimethylaminobenzaldehyde	$< 0{\cdot}1$

Some doubt has recently been expressed as to the validity of the ionic mechanism for the Cannizzaro reaction on the ground that it is catalysed by peroxides.‡ Haber and Willstätter suggested a radical-chain mechanism for the reaction and recently a modified scheme of this kind has been put forward by Weiss.§ The only evidence that the reaction necessarily involves free radicals is an assertion by Kharasch|| in a preliminary note that no reaction occurs if peroxides are removed completely from the reactants. Since after a lapse of nearly twelve years the promised details of this work have still not been published, it can be safely assumed that the observation proved later to be erroneous. Urushibaba and Takebayashi‡ found that peroxide-free benzaldehyde did undergo the reaction, and this has been confirmed by Alexander.‡

Weiss's argument, that *because* the reaction can be catalysed by peroxides (when a radical mechanism must operate) *therefore* the uncatalysed reaction must involve radicals, is fallacious. The additions of hydrogen bromide and halogens to olefines are strongly catalysed by peroxides, but the uncatalysed reactions are unquestionably ionic. Peroxide catalysis implies only that a radical mechanism is possible, not that the mechanism involves radicals in the absence of catalyst. This point is important since there is a strong tendency at the present time to accept peroxide catalysis as sufficient proof that a reaction is exclusively of radical type.

The Weiss mechanism suffers from a further objection. It does not even

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† The results are those of Weissberger and Haase, *J.C.S.* 1934, 535.

‡ Urushibaba and Takebayashi, *Bull. Chem. Soc. Japan*, 1937, **12**, 328. Recently Alexander (*J.A.C.S.* 1947, **69**, 289) has claimed that no peroxide catalysis occurs, but the discrepancy is probably due to use of different experimental conditions.

§ *Trans. Faraday Soc.* 1941, **37**, 782.

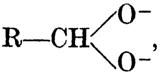
|| *J.A.C.S.* 1935, **57**, 1510.

account for the observed kinetics. Weiss's kinetic analysis of his own equations is incorrect. He assumes that the overall rate will be approximately that of the chain initiation reaction. This is untrue, even if the chains are short. Actually the chains must be long because very small amounts of peroxide can catalyse the reaction of a large amount of aldehyde (Urushibaba and Takebayashi, loc. cit.), and because the products of chain-termination are not present in isolable amounts. Weiss evades this last point by assuming only *one* of the three bimolecular chain termination processes possible in his scheme ($2\mathrm{RCHOH} \rightarrow ?$, $\mathrm{R{\cdot}CHOH}+\mathrm{R{\cdot}CO} \rightarrow ?$, $2\mathrm{RCO} \rightarrow ?$). Weiss incidentally calculates the kinetic expression wrongly from his equations. Without giving details of his scheme we may note the kinetic law that follows from it

$$\frac{d[\mathrm{RCOOH}]}{dt} = \frac{d[\mathrm{RCH_2OH}]}{dt} = \tfrac{1}{2}k_1 K_{\mathrm{OI}}[\mathrm{A}]^2[\mathrm{OH'}] + \\ +\tfrac{1}{2}k_1 K_{\mathrm{OI}}[\mathrm{RCHO}]^2[\mathrm{OH'}]\left\{1+\left(\frac{4k_5 k_6}{k_1 k_{\mathrm{OH}} k_7[\mathrm{OH'}]}\right)\right\}^{\frac{1}{2}}.$$

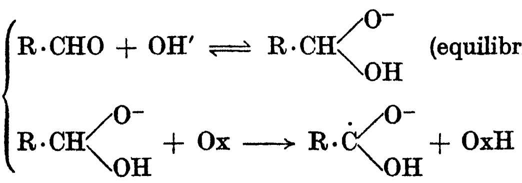
For long chains this reduces to an expression for the rate which does not agree with experiment:

$$\frac{d[\mathrm{RCOOH}]}{dt} \simeq \left(\frac{k_1 K_{\mathrm{OI}} k_5 k_6}{k_7}\right)^{\frac{1}{2}}[\mathrm{RCHO}]^2[\mathrm{OH'}]^{\frac{1}{2}}.$$

If the initiation reaction actually involves the doubly charged ion  $\mathrm{R{-}CH}\!\left\langle\begin{smallmatrix}\mathrm{O^-}\\ \mathrm{O^-}\end{smallmatrix}\right.$, the scheme does give third-order kinetics, but no reasonable modification will give an equation of the fourth order.

Incidentally Geib† has shown that the rate of the fourth-order reaction with furfural is unaffected by a variety of oxidizing agents and radical inhibitors, including potassium persulphate, permanganate, chlorate and nitrate, sodium sulphite, hydroquinone, diphenylamine, hydroxylamine, and ferrous salts. The reaction is unquestionably of ionic, not radical, type.

The radical-catalysed Cannizzaro reaction is almost certainly of the third order, since earlier investigators, who did not rigidly exclude peroxide, obtained third-order kinetics using benzaldehyde. The following scheme seems to account very well for the observed facts.‡



$$\text{Initiation}\begin{cases}\mathrm{R{\cdot}CHO} + \mathrm{OH'} \rightleftharpoons \mathrm{R{\cdot}CH}\!\left\langle\begin{smallmatrix}\mathrm{O^-}\\ \mathrm{OH}\end{smallmatrix}\right. & \text{(equilibrium constant } K_1) \quad (1)\\ \mathrm{R{\cdot}CH}\!\left\langle\begin{smallmatrix}\mathrm{O^-}\\ \mathrm{OH}\end{smallmatrix}\right. + \mathrm{Ox} \longrightarrow \mathrm{R{\cdot}\dot{C}}\!\left\langle\begin{smallmatrix}\mathrm{O^-}\\ \mathrm{OH}\end{smallmatrix}\right. + \mathrm{OxH} & (2)\end{cases}$$

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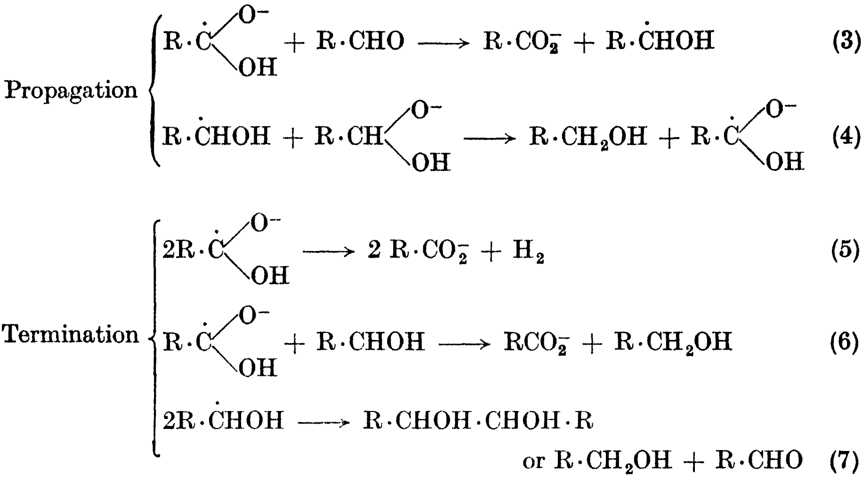
† *Z. phys. Chem.* 1934, A 169, 41.

‡ For a general account of radical chain reactions and their kinetics see Chapter XIII. It is, however, convenient to treat the Cannizzaro reaction as a whole, so the catalysed reaction is discussed here.



Propagation

$$\mathrm{R\cdot\dot{C}}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right. + \mathrm{R\cdot CHO} \longrightarrow \mathrm{R\cdot CO_2^-} + \mathrm{R\cdot\dot{C}HOH} \qquad (3)$$

$$\mathrm{R\cdot\dot{C}HOH} + \mathrm{R\cdot CH}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right. \longrightarrow \mathrm{R\cdot CH_2OH} + \mathrm{R\cdot\dot{C}}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right. \qquad (4)$$

Termination

$$2\mathrm{R\cdot\dot{C}}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right. \longrightarrow 2\,\mathrm{R\cdot CO_2^-} + \mathrm{H_2} \qquad (5)$$

$$\mathrm{R\cdot\dot{C}}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right. + \mathrm{R\cdot\dot{C}HOH} \longrightarrow \mathrm{RCO_2^-} + \mathrm{R\cdot CH_2OH} \qquad (6)$$

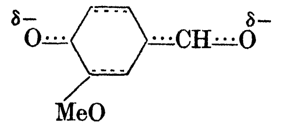
$$2\mathrm{R\cdot\dot{C}HOH} \longrightarrow \mathrm{R\cdot CHOH\cdot CHOH\cdot R} \text{ or } \mathrm{R\cdot CH_2OH} + \mathrm{R\cdot CHO} \qquad (7)$$

Both propagation reactions should be exothermic, since the resonance energy of the ion-radical $\mathrm{R—C}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right.$ will be considerable, yet less than that of the symmetrical ion $\mathrm{R\cdot CO_2^-}$. Unfortunately no explicit expression for the overall rate can be calculated from this scheme (which is formally identical with the general scheme given on p. 268) without simplifying assumptions. However, the termination reaction (5), involving the mutual reaction of ions of like charge, should be relatively unimportant. If also reaction (4) is faster than (3), the concentration of the ion-radical will be greater than that of $\mathrm{R\cdot\dot{C}HOH}$, and if reaction (5) is slow, (6) will be the main chain-termination process. For long chains the scheme then gives the rate to be

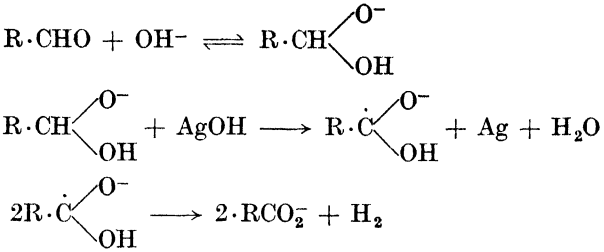
$$\frac{d[\mathrm{RCOOH}]}{dt} = \left(\frac{k_1 k_2 k_3 k_4}{k_6}\right)^{\frac{1}{2}}[\mathrm{R\cdot CHO}]^{\frac{3}{2}}[\mathrm{OX}]^{\frac{1}{2}}[\mathrm{OH'}] \equiv K[\mathrm{R\cdot CHO}]^2[\mathrm{OH'}]$$

as experiment requires (if the catalyst is aldehyde peroxide, its concentration is proportional to that of aldehyde). The alternative termination reactions give similar expressions with different powers of (OH′) (1·5 with equation (5), 0·5 with equation (7)).

If reaction (4) is faster than (3), it is probably also more exothermic. This would imply that the resonance energies of $\mathrm{R\cdot\dot{C}}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right.$ and $\mathrm{RCO_2^-}$ are nearly the same, which seems very reasonable. In that case mesomeric stabilization of the original aldehyde may make (3) sufficiently endothermic to interrupt the chain. Since the $\mathrm{R\cdot\dot{C}}\left\langle\begin{matrix}\mathrm{O^-}\\ \mathrm{OH}\end{matrix}\right.$ radicals will then not be removed by (3), reaction (5) will come into operation. This effect is well seen in the case of vanillin[†] which in alkali forms the mesomeric ion:



If an oxidant (AgOH) is added, vanillic acid and hydrogen are formed quantitatively, only one-half equivalent of oxidant being consumed.

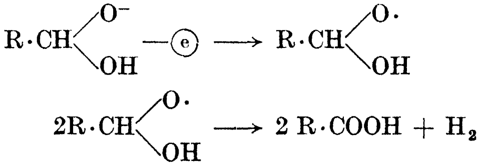


$$R{\cdot}CHO + OH^- \rightleftharpoons R{\cdot}CH\begin{matrix}\diagup O^- \\ \diagdown OH\end{matrix}$$

$$R{\cdot}CH\begin{matrix}\diagup O^- \\ \diagdown OH\end{matrix} + AgOH \longrightarrow R{\cdot}\dot{C}\begin{matrix}\diagup O^- \\ \diagdown OH\end{matrix} + Ag + H_2O$$

$$2R{\cdot}\dot{C}\begin{matrix}\diagup O^- \\ \diagdown OH\end{matrix} \longrightarrow 2{\cdot}RCO_2^- + H_2$$

The same reaction had been observed earlier in the case of formaldehyde by several authors.[‡] Here the reaction (3) will be slow because in water the equilibrium $CH_2O + H_2O \rightleftharpoons CH_2(OH)_2$ reduces the concentration of CH_2O greatly. A similar effect is observed in the anodic oxidation of aldehydes in alkali.[§] Here the first step is presumably an electron transfer, giving a neutral radical, and since the local concentration of such radicals near the anode will be high, they disproportionate to the corresponding carboxylic acid and hydrogen by a bimolecular reaction.

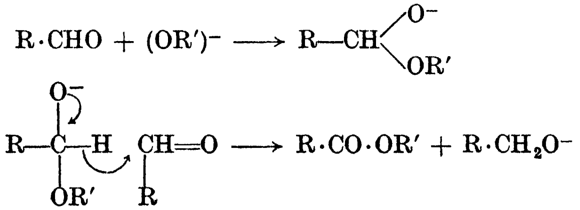


$$R{\cdot}CH\begin{matrix}\diagup O^- \\ \diagdown OH\end{matrix} - ⓔ \longrightarrow R{\cdot}CH\begin{matrix}\diagup O\cdot \\ \diagdown OH\end{matrix}$$

$$2R{\cdot}CH\begin{matrix}\diagup O\cdot \\ \diagdown OH\end{matrix} \longrightarrow 2\,R{\cdot}COOH + H_2$$

The Titschenko reaction

Aromatic aldehydes react with sodium alkoxides to give esters by a disproportionation similar to the Cannizzaro reaction. Sodium alkoxide is regenerated in the reaction so that small amounts can act catalytically. Analogy with the Cannizzaro reaction suggests the mechanism



$$R{\cdot}CHO + (OR')^- \longrightarrow R{-}CH\begin{matrix}\diagup O^- \\ \diagdown OR'\end{matrix}$$

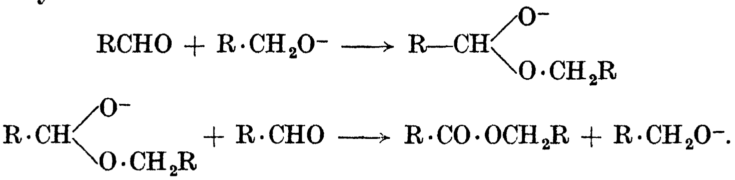
$$R{-}\underset{OR'}{\overset{O^-}{C}}{-}H \quad \underset{R}{CH{=}O} \longrightarrow R{\cdot}CO{\cdot}OR' + R{\cdot}CH_2O^-$$

[†] Pearl, *J.A.C.S.* 1945, **67**, 1628; 1946, **68**, 429, 1100, 2180.

[‡] Loew, *Ber.* 1887, **20**, 144; Müller, *Annalen*, 1920, **420**, 241; Geisow, *Ber.* 1904, **37**, 515; Lyford, *J.A.C.S.* 1907, **29**, 1227.

[§] Müller, loc. cit.

followed by



$$RCHO + R{\cdot}CH_2O^- \longrightarrow R{-}CH\begin{cases}O^-\\O{\cdot}CH_2R\end{cases}$$

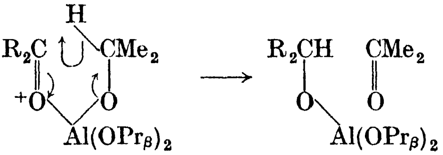
$$R{\cdot}CH\begin{cases}O^-\\O{\cdot}CH_2R\end{cases} + R{\cdot}CHO \longrightarrow R{\cdot}CO{\cdot}OCH_2R + R{\cdot}CH_2O^-.$$

No radical catalysis has been observed; none would be expected if the scheme suggested previously for the catalysed Cannizzaro reaction is correct, since in this case one of the chain propagation reactions would involve an improbable transfer of an alkyl group instead of a hydrogen atom.

The Meerwein-Ponndorf and Oppenauer reactions

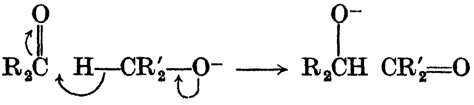
Aluminium alkoxides react reversibly with ketones and aldehydes to give a new carbonyl compound and alcohol. There is no definite evidence for the mechanism, but from analogy the following scheme seems probable:

$$R_2C{=}O + Al(OPr_\beta)_3 \longrightarrow R_2C{=}\overset{+}{O}{-}\overset{-}{Al}(OPr_\beta)_3$$

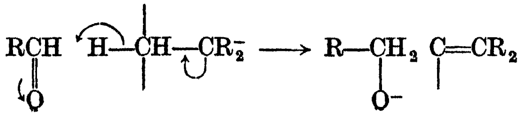


The reaction again involves a transfer of negative hydrogen. Aluminium alkoxides are especially effective since they are relatively weak bases and so do not often bring about side-reactions, such as aldol condensations of the carbonyl compound; and because they are powerful cationoid reagents which can form acceptor bonds with the carbonyl oxygen, the resulting complex being electronically and sterically favourable to the transfer of H^-.

In certain cases sodium alkoxides can reduce carbonyl compounds, again presumably by transfer of H^-:

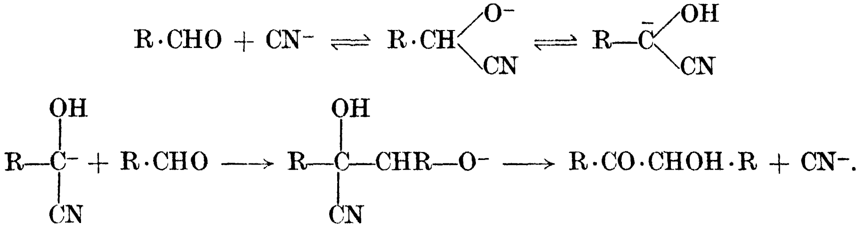


The reaction is analogous to the reduction of neopentyl iodide by sodium ethoxide (p. 82). The abnormal action of Grignard reagents in reducing certain aldehydes to alcohols is probably similar:



The benzoin reaction

The catalytic condensation of aromatic aldehydes by CN^- also takes place by a transfer of negative hydrogen; Lapworth[†] suggested the mechanism:

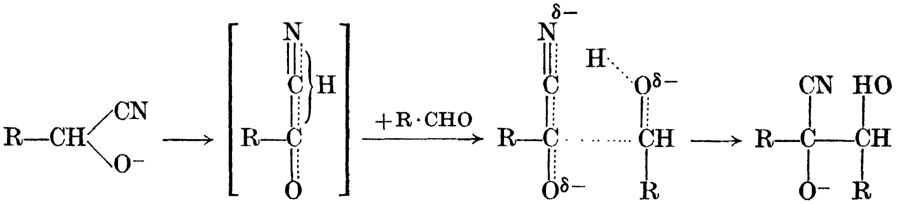


$$R\cdot CHO + CN^- \rightleftharpoons R\cdot CH{<}^{O^-}_{CN} \rightleftharpoons R—\bar{C}{<}^{OH}_{CN}$$

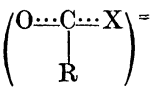
$$R—\overset{OH}{\underset{CN}{C^-}} + R\cdot CHO \longrightarrow R—\overset{OH}{\underset{CN}{C}}—CHR—O^- \longrightarrow R\cdot CO\cdot CHOH\cdot R + CN^-.$$

This mechanism requires that the reaction be of third order, as observed,[‡] the rate being given by $k[RCHO]^2[CN^-]$ if the rate-determining step is the addition of the intermediate anion to the second aldehyde molecule.

This scheme must be essentially correct, but it does not explain the specific activity of cyanide. It is therefore more likely that the (aldehyde—CN^-) adduct rearranges not to $R\cdot C^-{<}^{OH}_{CN}$ but to a π-complex in which hydrogen is attached by a molecular bond to the mesomeric system $(O\cdots\underset{R}{C}\cdots C\cdots N)^-$. During the condensation with the second aldehyde molecule, this non-localized proton can attack the carbonyl oxygen simultaneously with the anionoid attack on the carbonyl carbon.



The electronic requirements for the catalyst are therefore that it should be a strongly anionoid reagent, but that the corresponding radical should be a strongly cationoid substituent; because if the catalyst is X^-, the ion



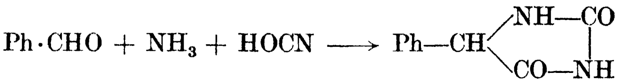
$$\left(O\cdots\underset{R}{C}\cdots X\right)^=$$

must be electronically possible, since the π-complex effectively contains this ion linked to a proton by a molecular bond. Only the cyanide ion fulfils these requirements. Incidentally it is difficult to see how the Lapworth mechanism could be reversible, but the π-complex mechanism, in which hydrogen transfer accompanies addition to the carbonyl, might well be so. Recently Jesus Romo† has shown that benzoin can indeed be converted to benzaldehyde, since it gives phenylhydantoin on treatment with ammonium carbonate and potassium cyanate in alcohol.

[†] *J.C.S.* 1903, **83**, 995.

[‡] Bredig and Stern, *Z. Elektrochem.* 1904, **10**, 582.

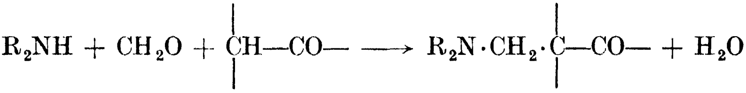
$$\mathrm{Ph\cdot CO\cdot CHOH\cdot Ph} \longrightarrow 2\,\mathrm{PhCHO}$$



The mechanism of the reverse reaction is not certain, but it probably involves a preliminary attack on carbonyl by cyanate ion. It is amusing that benzil under the same conditions gives phenylhydantoin and ethyl benzoate.

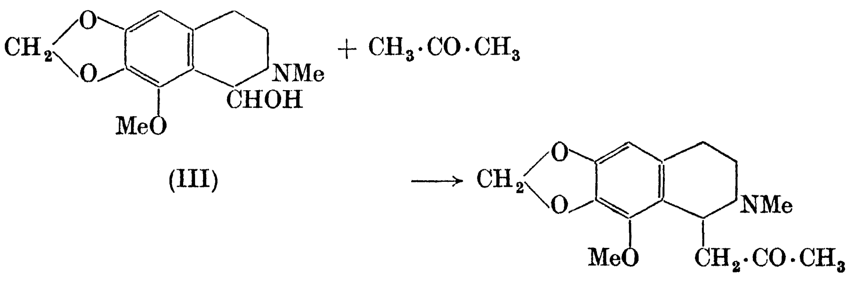
The Mannich reaction,‡ syntheses under 'physiological conditions'

Secondary amines condense with formaldehyde and ketones to give basic ketones.



$$\mathrm{R_2NH + CH_2O + \overset{|}{\underset{|}{C}}H{-}CO{-}} \longrightarrow \mathrm{R_2N\cdot CH_2\cdot \overset{|}{\underset{|}{C}}{-}CO{-} + H_2O}$$

In certain cases the reaction also occurs with primary or secondary amines or with other aldehydes. Acid is required as catalyst. The mechanism of the reaction is uncertain; but since Hope and Robinson§ found that cotarnine (III) readily condenses with acetone, nitromethane, and other compounds containing acidic hydrogen, and since this reaction has been shown to occur very generally with other α-hydroxyamines, it seems likely that a methylolamine is an intermediate in the Mannich reaction.

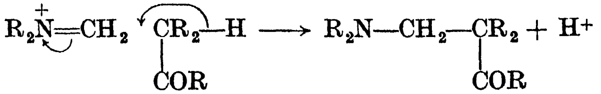


(III)

Acid is required as a catalyst, so the methylolamine is probably first converted into a reactive methyleneammonium salt, and this condenses either with the ketone itself, or with the enol form of the ketone formed catalytically by the acid present.

$$\mathrm{R_2NH + CH_2O} \longrightarrow \mathrm{R_2N\cdot CH_2OH} \xrightarrow{\mathrm{H^+}} \mathrm{R_2\overset{+}{N}{=}CH_2}$$

(*a*)



$$\mathrm{R_2\overset{+}{N}{=}CH_2 \quad \underset{\displaystyle COR}{CR_2}{-}H} \longrightarrow \mathrm{R_2N{-}CH_2{-}\underset{\displaystyle COR}{CR_2} + H^+}$$

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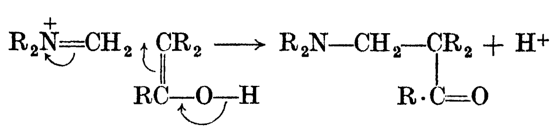
† *Ciencia* (Mexico), 1943, **4**, 216.

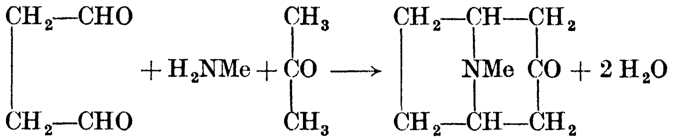
‡ See Blicke, *Organic Reactions*, **1**, 303.

§ *J.C.S.* 1911, **99**, 2114; 1913, **103**, 361.

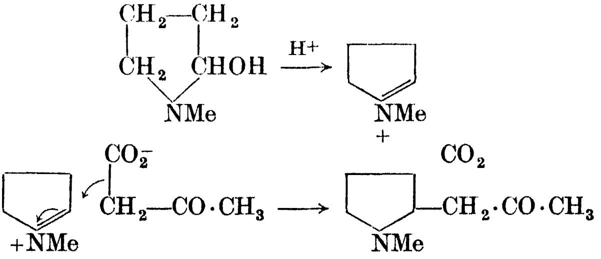
(*b*)



This mechanism led Robinson to propose his well-known theory of the phytosynthesis of alkaloids† which was confirmed by a spectacular synthesis of tropinone *in vitro* from materials which might reasonably occur in plant sap.

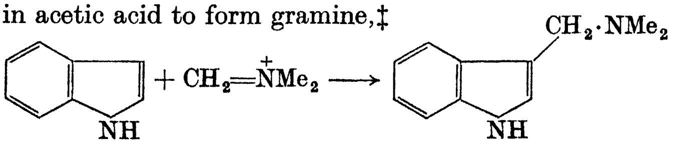


The process is a double Mannich reaction, and it was found to occur still more readily with acetonedicarboxylic acid. Reactions of this type with β-ketoacids have been studied in detail by Schöpf and his collaborators, who have shown that they proceed readily in cold dilute neutral solution, and have synthesized a number of naturally occurring alkaloids in this way. They found that the yields were highest in neutral solution, and that the β-ketoacids used always underwent simultaneous decarboxylation, although the parent acids were comparatively stable under the same conditions. This suggests that the methyleneammonium salt reacts with the anion of the acid; for instance, the synthesis of hygrine may be represented:



In acid solution, the acid is not present as its anion, while in alkaline solution the methyleneammonium salt is converted to a less reactive methylolamine. It is interesting that the sodio derivatives of β-ketoesters will condense with methylolamines to give products analogous to those of the Mannich reaction, probably by S_2 replacements of hydroxyl.

The general mechanisms for the reactions are confirmed by analogous condensations of aldehydes and amines with strongly anionoid aromatic rings. Thus indole, formaldehyde, and dimethylamine condense quantitatively in acetic acid to form gramine,‡



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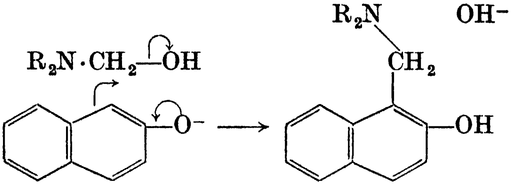
† Ibid. 1917, **111**, 876; *The Molecular Architecture of Some Plant Products*, IXth Congress of Pure and Applied Chemistry, Madrid, 1934.

‡ Kühn and Stein, *Ber.* 1937, **70**, 567.

implying that a cationoid intermediate is formed from the amine and aldehyde; while the condensation of phenols under alkaline conditions with methylolamines suggests an S_2 replacement of hydroxyl by a strongly basic phenoxide ion:†



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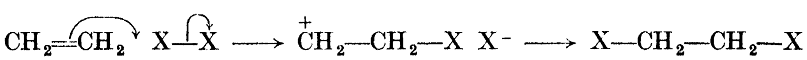
† Cf. Decombe, *Compt. rend.* 1933, **196**, 866.

CHAPTER VIII

REACTIONS OF CARBON—CARBON MULTIPLE BONDS

THE classical picture of halogen addition to olefines postulated a simultaneous addition of both atoms in the halogen molecule. This view was disproved by the discovery† that in such reactions *trans* addition occurs; thus maleic acid with bromine gives almost exclusively racemic dibromosuccinic acid, while direct addition of a bromine molecule to the double bond would give the *cis* adduct, *meso*-dibromosuccinic acid. This observation suggests that addition takes place in two steps. Moreover, the reaction involves ionic intermediates since it takes place only in a polar environment; the addition of bromine vapour to ethylene gas takes place entirely on the glass walls of the reaction vessel‡ and is greatly retarded if the walls are coated with paraffin wax which is non-polar. A coating of some polar substance such as stearic acid leads to an increase in the rate.

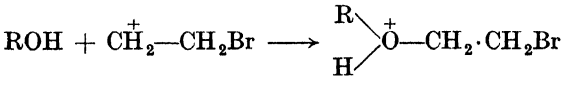
Robinson suggested that the initial step in the addition was a cationoid attack on the olefine by halogen to form a haloethyl cation, the latter then combining with the halogen anion formed in the first step.



$$CH_2{=}CH_2\ X{-}X \longrightarrow \overset{+}{C}H_2{-}CH_2{-}X\ X^- \longrightarrow X{-}CH_2{-}CH_2{-}X$$

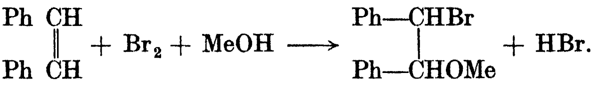
This mechanism is supported by three lines of evidence.

Firstly, when ethylene reacts with bromine in an aqueous solution of chloride or nitrate, bromoethyl chloride or nitrate is formed;§ the intermediate carbonium ion combines with a foreign anion. A similar attack on solvent molecules by the intermediate accounts well for the formation of bromohydrins from olefines with bromine in water, and of bromoethers with bromine in alcohol.



$$ROH + \overset{+}{C}H_2{-}CH_2Br \longrightarrow \begin{matrix} R \\ H \end{matrix}\!>\!\overset{+}{O}{-}CH_2{\cdot}CH_2Br$$

The latter reaction has been proved|| not to proceed via an intermediate alkyl hypobromite as earlier workers had supposed. When stilbene reacts with bromine in methanol, a bromoether can be isolated:



$$\begin{matrix} Ph\ CH \\ \| \\ Ph\ CH \end{matrix} + Br_2 + MeOH \longrightarrow \begin{matrix} Ph{-}CHBr \\ | \\ Ph{-}CHOMe \end{matrix} + HBr.$$

Now if methyl hypobromite is an intermediate it must be formed by the reversible reaction

$$2MeOH + Br_2 \rightleftharpoons MeOBr + Br^- + MeOH_2^+$$

---

† McKenzie, *Proc. Chem. Soc.* 1911, **27**, 150; *J.C.S.* 1912, **101**, 1196; Frankland, ibid., p. 673.

‡ Norrish, ibid. 1923, **123**, 3006.

§ Francis, *J.A.C.S.* 1925, **47**, 2340.

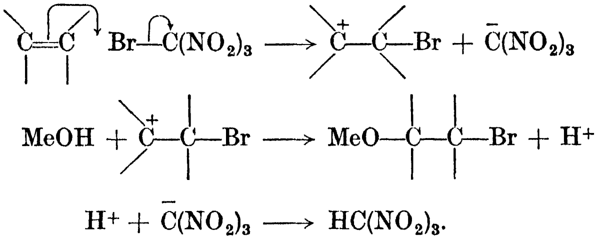
|| Bartlett and Tarbell, ibid. 1936, **58**, 466.

(HBr is a strong acid in methanol and will be completely dissociated). The equilibrium concentration of MeOBr will be given by

$$[\mathrm{MeOBr}] = K\frac{[\mathrm{MeOH}]^2[\mathrm{Br_2}]}{[\mathrm{Br^-}][\mathrm{MeOH_2^+}]},$$

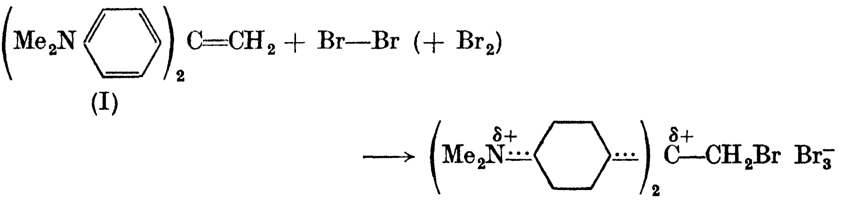
and will therefore be reduced by addition of acid. Acid would therefore reduce the rate of reaction if MeOBr were an intermediate; and this effect was not observed. Incidentally alkyl hypohalites react more slowly with olefines than does a mixture of the corresponding halogen and alcohol, again proving that hypohalite is not an intermediate in the latter reaction.

Secondly, compounds containing 'positive halogen' can bring about addition to olefines. Thus with bromotrinitromethane in methanol, olefines give bromoethers;† a reaction best represented as:



Other analogous halogen compounds such as bromopicrin, ethyl bromonitromalonate, and N-bromacetamide react similarly.

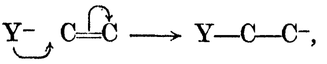
Thirdly, the intermediate cation has actually been isolated in one case where it is stabilized by mesomerism.‡ The addition of bromine to the olefine (I) gives the salt (II) where the *para* nitrogens share the positive charge with the ethylenic carbon.



(I)

(II)

This simple theory of addition to olefines suffers, however, from two defects. Firstly, it does not explain why olefines react only with cationoid reagents. The C=C bond is symmetrical and should equally easily add active anions:



particularly since ions of the type R_3C^- seem at least as stable as R_3C^+. Such anionoid additions are never observed. And secondly, the theory does not explain the exclusive *trans* addition of halogen to olefines. The intermediate cation would be symmetrical and should give a mixture of *cis* and *trans* adducts.

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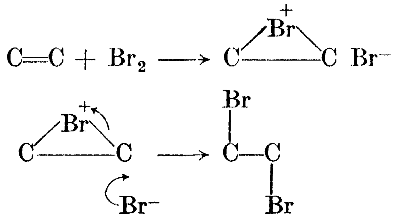
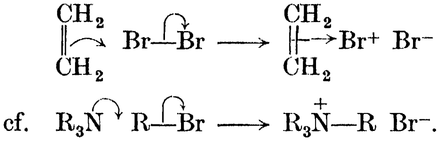
† Schmidt, Ascherl, and v. Knilling, *Ber.* 1926, **59**, 1876.

‡ Pfeffer and Wizinger, *Annalen*, 1928, **461**, 132.

Roberts and Kimball† pointed out that the latter effect could be explained if the intermediate ion had a cyclic structure, the subsequent reaction with the anion being an S_2 replacement in which the ring opens and the *trans* adduct is formed:

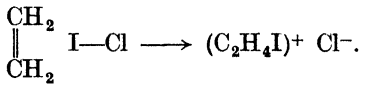


The exclusive anionoid reactivity of olefines can then be explained if the intermediate 'cyclic' cation is in fact a π-complex in which a bromous cation is linked to the π-electrons of the C=C bond (cf. p. 17). Its formation will be electronically analogous to the formation of a quaternary ammonium salt from a tertiary amine and alkyl bromide:



The corresponding reaction with an anion is impossible since ethylene has no vacant electron orbital of low energy and cannot therefore act as an electron acceptor without actual fission of the π-bond. (The latter process does occur in reactions with atoms or radicals; Chapters XIII, XIV.)

Further evidence is provided by the orientation of the products from the addition of iodine chloride to unsymmetrical olefines. These reactions resemble the normal halogen additions and the intermediate cation is presumably formed by addition of the less electronegative halogen to the olefine:



$$\begin{array}{l} CH_2 \\ \| \\ CH_2 \end{array} \quad I\text{—}Cl \longrightarrow (C_2H_4I)^+ \; Cl^-.$$

Now if the cation were a simple cyclic compound, as Roberts and Kimball suggest, the subsequent S_2 replacement should take place at the end of the olefine most positively substituted, since S_2 replacements are accelerated by positive substituents, and the chlorine should appear there in the products. Actually the observed orientation is just the opposite. This result can be explained in terms of the π-complex theory. In the π-complex substituents will polarize the double bond; therefore in an unsymmetrical olefine the I^+ cation will be attached unsymmetrically, being closer to the more negative end of the bond—i.e. to the end with more positive or less negative substituents. Reaction with an anion should then occur more readily at the other carbon since a smaller movement of groups will be required and the activation energy should therefore be less.

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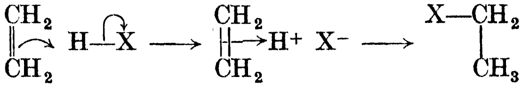
† *J.A.C.S.* 1937, 59, 947.

Other cationoid reactions of olefines probably take place through π-complex intermediates; for instance, the addition of hydrogen halides to olefines.

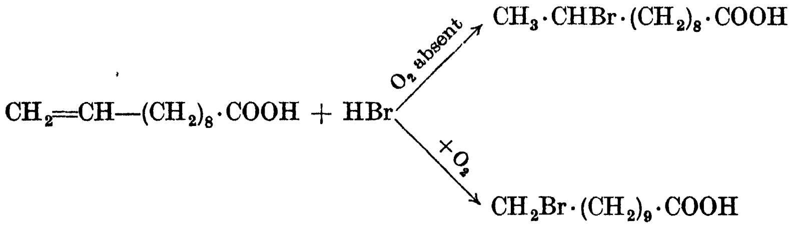


$$\begin{matrix} CH_2 \\ \| \\ CH_2 \end{matrix} \; H{-}X \longrightarrow \begin{matrix} CH_2 \\ \| \\ CH_2 \end{matrix} \!\rightarrow H^+ \; X^- \longrightarrow \begin{matrix} X{-}CH_2 \\ | \\ CH_3 \end{matrix}$$

Here again the halogen anion attacks the more negative end of the double bond, and therefore in the addition of hydrogen halide to an ethylene derivative containing only negative substituents, the product contains halogen attached to the more substituted carbon (Markownikoff's rule). The rule naturally fails in positively substituted ethylenes; thus acrylic acid gives β-halopropionic acids, the less substituted olefinic carbon now being the more negative (or less positive).

The peroxide effect

Certain additional exceptions to Markownikoff's rule have recently been observed in the addition of hydrogen bromide to olefines. In the absence of oxygen and peroxides 'normal' addition takes place slowly, but in their presence a much faster 'abnormal' addition gives products violating Markownikoff's rule. This phenomenon, which has been called the peroxide effect, was first established by Urushibaba and Robinson[†] for the addition of hydrogen bromide to undecylenic acid.


$CH_3 \cdot CHBr \cdot (CH_2)_8 \cdot COOH$
O_2 absent
$CH_2{=}CH{-}(CH_2)_8 \cdot COOH + HBr$
$+O_2$
$CH_2Br \cdot (CH_2)_9 \cdot COOH$

It has since been fully investigated and shown to be very general.[‡] Other hydrogen halides do not show the effect.

The mechanism was first indicated by experiments on the isomerization of *cis* to *trans* stilbene.[§] This reaction was known to be catalysed by bromine in sunlight but not in the dark, the active catalyst being atomic bromine produced by photo-chemical dissociation of bromine into atoms (cf. p. 255). In the dark and in absence of peroxides, hydrogen bromide did not isomerize stilbene; but if oxygen, or even air, were admitted, isomerization readily took place. This experiment indicated strongly that hydrogen bromide is oxidized by oxygen to bromine atoms, and that these then catalyse the interconversion. It therefore seemed likely that bromine atoms are also intermediates in the abnormal addition of hydrogen bromide to olefines.[†]

[†] *Chem. Ind.* **1933, 11,** 219.

[‡] For a summary see Smith, *Ann. Rep. Chem. Soc.* 1939, 219.

[§] Kharasch, Mansfield, and Mayo, *J.A.C.S.* 1937, 59, 1155.

The mechanism proposed by Kharasch and his collaborators involves a chain reaction (cf. Chapter XIII).

$$\begin{array}{ll}
\text{Initiation} & \mathrm{HBr + Ox \rightarrow Br\cdot + HOx\ (Ox = catalyst)} \\[1ex]
\text{Propagation} & \begin{cases} \mathrm{Br\cdot + CR_2{=}CR_2 \rightarrow Br{-}CR_2{-}CR_2\cdot} \\ \mathrm{BrCR_2{-}CR_2\cdot + Br_2 \rightarrow Br\cdot CR_2\cdot CR_2Br + Br\cdot} \end{cases} \\[1ex]
\text{Termination} & \begin{cases} \mathrm{2Br\cdot \rightarrow Br_2} \\ \mathrm{Br\cdot + BrCR_2\cdot CR_2\cdot \rightarrow BrCR_2\cdot CR_2Br} \\ \mathrm{2BrCR_2\cdot CR_2\cdot \rightarrow BrCR_2\cdot CR_2\cdot CR_2\cdot CR_2\cdot Br} \end{cases}
\end{array}$$

Since the propagation reactions regenerate a bromine atom, one such atom may bring about the reaction of hundreds or thousands of molecules of olefine. This mechanism explains why 'inhibitors' (that is, substances like hydroquinone which can react with atoms or radicals to give inert products) reduce the rate of peroxide-catalysed addition. It also accounts for the failure of other hydrogen halides to give abnormal addition; hydrogen chloride is not easily oxidized to atomic chlorine, while iodine atoms are too unreactive to add to the C=C bond.

Two further lines of evidence have been given for the intervention of radical intermediates. Bockmüller and Pfeuffer[‡] found that bromine and excess oxygen react with various olefines to form peroxides; thus allyl bromide gives *bis*dibrom*iso*propyl peroxide.

$$\mathrm{BrCH_2{-}CH{=}CH_2 + Br\cdot \rightarrow BrCH_2{-}\overset{\bullet}{C}H{-}CH_2Br}$$

$$\mathrm{2\ (Br{-}CH_2{-}\overset{\bullet}{C}H{-}CH_2Br) + O_2 \rightarrow (BrCH_2)_2CH\cdot O{-}O\cdot CH(CH_2Br)_2}$$

Evidently *bis*brom*iso*propyl radicals are intermediates. Secondly, stilbene with hydrogen bromide and oxygen in the dark gives a quantitative yield of stilbene dibromide;[§] a radical mechanism is indicated since oxygen does not react with hydrogen bromide under these conditions.

This latter observation raises a further point: hydrogen bromide is not oxidized by oxygen in the dark, but the mixture reacts rapidly with olefines. Winstein and Lucas[||] therefore suggested that the oxygen first forms a compound with the olefine, the compound then reacting with HBr. These authors, however, favoured an ionic mechanism which explained neither the effect of inhibitors nor the failure of other hydrogen halides to react likewise. Conn, Kistiakowsky, and Smith† suggested that the intermediate rather oxidizes HBr to Br atoms, starting radical chains. This certainly seems a more plausible view. The olefine —O_2 adduct is probably a π-complex, and a similar intermediate has been postulated in the uncatalysed auto-oxidation of linoleic acid (p. 275).

[†] Kharasch, Engelmann, and Mayo, *J. Org. Chem.* 1937, **2**, 288; Hey and Waters, *Chem. Rev.* 1937, **21**, 203.

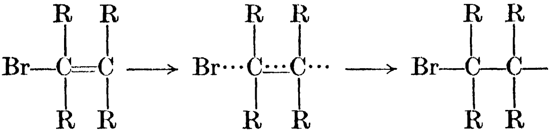
[‡] *Annalen*, 1939, **537**, 178.

[§] Urushibaba and Simamura, *Bull. Chem. Soc. Japan*, 1939, **14**, 323.

[||] *J.A.C.S.* 1938, **60**, 843.

Orientation of peroxide-catalysed addition

The orientation of the product from HBr and an unsymmetrical olefine in presence of peroxides depends on the way bromine atoms attach themselves to the double bond. The transition states are of the type (III)



$$\mathrm{Br{-}\overset{R}{\underset{R}{C}}{=}\overset{R}{\underset{R}{C}}} \longrightarrow \mathrm{Br\cdots\overset{R}{\underset{R}{C}}\overset{\cdot\cdot\cdot}{=}\overset{R}{\underset{R}{C}}\cdots} \longrightarrow \mathrm{Br{-}\overset{R}{\underset{R}{C}}{-}\overset{R}{\underset{R}{C}}{-}}$$

(III)

where the terminal carbon is already partly a radical centre. This centre will be stabilized by conjugation with $\pm$E substituents (p. 243), in fact by almost any substituent; therefore in an unsymmetrical olefine the more stable transition state will be the one in which bromine attacks the *less* substituted ethylenic carbon. The product of addition therefore has halogen attached to the less substituted carbon, violating Markownikoff's rule.

Since the effect of $+$E and $-$E substituents are here the same, positively substituted ethylenes, such as acrylic acid, will add hydrogen bromide in the same way both in the catalysed and uncatalysed reactions. This has been taken as evidence that the strongly polar carboxyl substituent favours ionic addition under all circumstances, a view which seems unlikely since the facile radical-catalysed polymerization of such compounds shows that they can react readily with radicals and so presumably also with atoms (Chapter XIV). In this case we would expect the peroxide-catalysed and ionic additions to give similar products.

Other analogous reactions

Although other hydrogen halides do not show the peroxide effect, a similar non-Markownikoff addition has been observed when thiols‡ or bisulphites§ react with olefines in presence of air or other oxidizing reagents. No addition takes place in the absence of oxidants, and the reaction can moreover be inhibited by hydroquinone. It seems clear that a radical-chain mechanism is again involved:

$$O_2 + HSO_3^- \rightarrow O_2H + {-}SO_3^-$$
$$C{=}C + {-}SO_3^- \rightarrow {-}C{-}C{-}SO_3^-$$
$$SO_3^-H + {-}C{-}C{-}SO_3^- \rightarrow H{-}C{-}C{-}SO_3^- + {-}SO_3^-, \quad \text{etc.}$$

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† *J.A.C.S.* 1938, **60**, 2770.

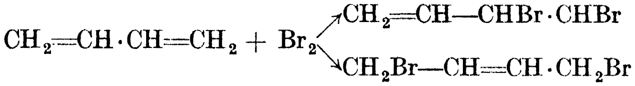
‡ Kharasch, May, and Mayo, *Chem. Ind.* 1938, **16**, 774; *J. Org. Chem.* 1938, **3**, 175.

§ Kharasch, Read, and Mayo, *Chem. Ind.* 1938, **16**, 752.

The addition of halogen can also occur by a similar mechanism, but this together with other analogous reactions will be discussed in Chapter XIII.

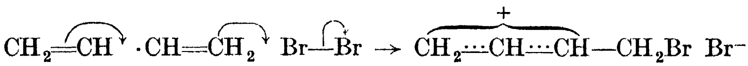
Addition to conjugated dienes

Addition of bromine to butadiene gives a mixture of 1:2 and 1:4 dibromides:



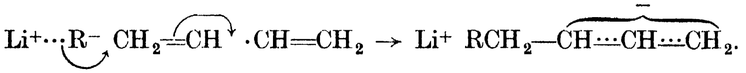
$$CH_2{=}CH\cdot CH{=}CH_2 + Br_2 \begin{array}{l} \nearrow CH_2{=}CH{-}CHBr\cdot CHBr \\ \searrow CH_2Br{-}CH{=}CH\cdot CH_2Br \end{array}$$

This phenomenon is a very general one in compounds containing two or more conjugated double bonds. The explanation is very simple; the reaction takes place in two stages as usual, but here the intermediate cation is mesomeric and can react with the anion in more than one way.



$$CH_2{=}CH\cdot CH{=}CH_2\ Br{-}Br \rightarrow \overbrace{CH_2{\cdots}CH{\cdots}CH}^{+}{-}CH_2Br\ Br^-$$

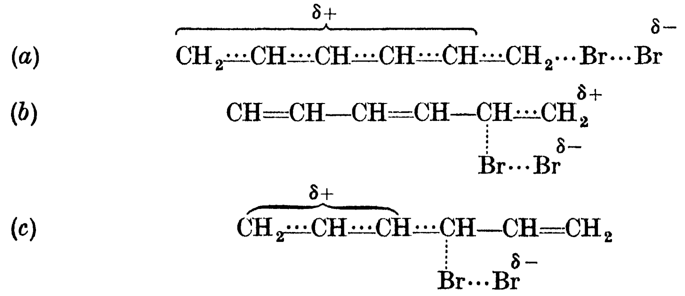
Since the resonance energy of the allyl cation is considerable, the π-complex mechanism may here be relatively unfavourable; the intermediate probably has the simple structure indicated. It is interesting that a similar mesomeric anion could result from attack by an anion on a conjugated system, although a π-complex could not (p. 143); and indeed conjugated polyenes differ from simple olefines in being able to add active anions. Thus lithium alkyls will add to butadiene (cf. p. 282):



$$Li^+\cdots R^-\ CH_2{=}CH\cdot CH{=}CH_2 \rightarrow Li^+\ RCH_2{-}\overbrace{CH{\cdots}CH{\cdots}CH_2}^{-}.$$

Orientation of addition to conjugated systems

In normal addition to a conjugated system, the initial attack always takes place on a terminal carbon. The reason for this can easily be seen if we consider the transition states for the possible modes of addition to such a compound, e.g. hexatriene.



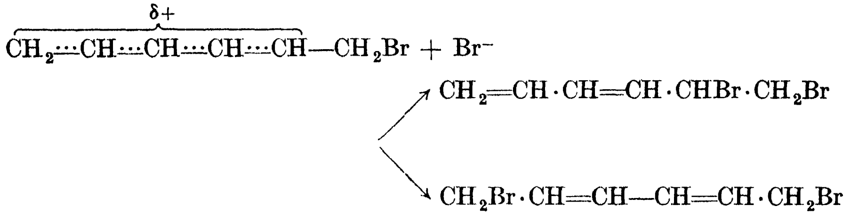
(a) $$\overbrace{CH_2{\cdots}CH{\cdots}CH{\cdots}CH{\cdots}CH{\cdots}CH_2}^{\delta+}\cdots Br\cdots Br^{\delta-}$$

(b) $$CH{=}CH{-}CH{=}CH{-}CH{\cdots}CH_2^{\delta+} \quad (CH\vdots Br\cdots Br^{\delta-})$$

(c) $$\overbrace{CH_2{\cdots}CH{\cdots}CH{\cdots}CH}^{\delta+}{-}CH{=}CH_2 \quad (CH\vdots Br\cdots Br^{\delta-})$$

In the first state (*a*) the positive charge is spread over five carbon atoms, in (*b*) over one, in (*c*) over three. Now quantum-mechanical calculation shows that of two mesomeric systems of similar type, the larger has the greater resonance energy. Since (*a*) has a larger mesomeric system than (*b*) or (*c*), it will be the most stable of the three and hence terminal attack on the conjugated system is favoured. It will also be seen that (*c*) is more stable than (*b*); this illustrates a general principle that in a conjugated system the most favoured points of attack, excluding the ends, are the atoms an odd number of places from either end; and a little consideration will show that the reactivity of such atoms in turn falls with increase in distance from an end of the conjugated chain.

Exactly the same arguments show that in the second step of the reaction the anion will attack preferentially a terminal atom in the mesomeric cationic system. Thus with hexatriene, 1:2 and 1:6 addition should predominate.



$$\overbrace{CH_2\cdots CH\cdots CH\cdots CH\cdots CH}^{\delta+}—CH_2Br + Br^- \begin{cases} \nearrow CH_2{=}CH\cdot CH{=}CH\cdot CHBr\cdot CH_2Br \\ \searrow CH_2Br\cdot CH{=}CH—CH{=}CH\cdot CH_2Br \end{cases}$$

That mode of addition is favoured which gives the most stable product. Now 1:2 addition gives a butadiene derivative in which one alkyl group ($CH_2Br\cdot CHBr\cdot$) can hyperconjugate with the double bonds, but the 1:6 adduct contains two such alkyl groups (CH_2Br). Therefore the latter mode of addition should be favoured—as it in fact is.†

An extension of this argument leads us to expect terminal addition to predominate in reactions of polyenes; Thiele, of course, showed long ago that this does happen.

The second step in these addition reactions resembles the recombination step in a tautomeric change. Indeed, the addition of bromine to conjugated systems is often complicated by anionotropy in the products; bromine can ionize reversibly from them to give mesomeric cations. Hence the ratio of the amounts of products formed may be determined by the anionotropic equilibrium between them rather than by their rates of formation from the common ion (cf. p. 106). In either case terminal addition will be favoured.

Reactions of the Michael type

Addition to a conjugated system containing a terminal hetero atom (e.g. acrolein, $CH_2\cdots CH\cdots CH\cdots O$, or acrylonitrile, $CH_2\cdots CH\cdots C\equiv N$) presents special features. Such compounds add cationoid reagents (Cl_2, HBr, etc.) normally, but differ from ordinary polyenes in being able to add a variety of relatively unreactive anions. These reactions resemble carbonyl additions; the latter are possible because one atom forming the double bond has a much larger electron affinity than the other, and a similar effect can be produced in the C=C bond by positive substitution of one carbon. The general mechanism may be written

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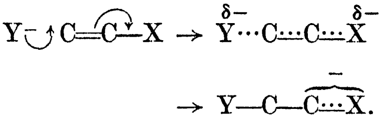
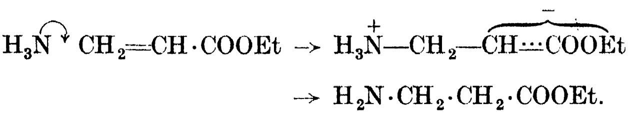
† Farmer, Laroia, Switz, and Thorpe, *J.C.S.* 1927, 2937.



$$Y\ C{=}C{-}X \rightarrow \overset{\delta-}{Y}\cdots C\overset{..}{\cdots}C\overset{..}{\cdots}\overset{\delta-}{X}$$
$$\rightarrow Y{-}C{-}\overset{-}{\overbrace{C\overset{..}{\cdots}X}}.$$

The classical example was the Michael addition of sodiomalonic ester and other related compounds to $\alpha{:}\beta$-unsaturated esters and ketones. The reaction is also shown by uncharged anionoid reagents, as in the addition of ammonia to ethyl acrylate:



$$H_3N\ CH_2{=}CH{\cdot}COOEt \rightarrow H_3\overset{+}{N}{-}CH_2{-}\overset{-}{\overbrace{CH\overset{..}{\cdots}COOEt}}$$
$$\rightarrow H_2N{\cdot}CH_2{\cdot}CH_2{\cdot}COOEt.$$

Naturally the ease of reaction is increased by positive and decreased by negative substituents; thus alkylidenecyanacetic esters add cyanide ion quite readily, although acrylic esters do not, and alkylacrylic esters are less reactive than acrylic ester itself.

Acetylene derivatives

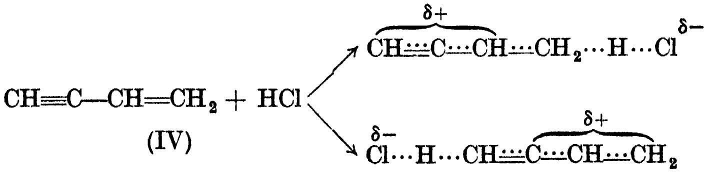
The addition reactions of acetylene resemble closely those of ethylene, since the two π-bonds in it are perpendicular to one another and are therefore electronically independent. However, acetylenes are somewhat more reactive than olefines, since the energy required to break one π-bond in an acetylene is less than that required to break the π-bond in an olefine:

$$E_{C\equiv C} - E_{C=C} = 45{\cdot}5 \text{ cals.}$$

$$E_{C=C} - E_{C-C} = 63{\cdot}5 \text{ cals.};$$

therefore addition reactions of acetylenes are the more exothermic.

The reactions of systems containing conjugated double and triple bonds present features of interest. Only one component of a triple bond can conjugate with an adjacent double bond. For example, vinylacetylene (IV) shows roughly the same reactivity as butadiene. If we write the transition states for the two modes of attack by hydrogen chloride,



(IV)

$$CH{\equiv}C{-}CH{=}CH_2 + HCl \nearrow \overset{\delta+}{\overbrace{CH\overset{..}{\cdots}C\overset{..}{\cdots}CH}}\overset{..}{\cdots}CH_2\cdots H\cdots \overset{\delta-}{Cl} \quad (a)$$
$$\searrow \overset{\delta-}{Cl}\cdots H\cdots CH\overset{..}{\cdots}\overset{\delta+}{\overbrace{C\overset{..}{\cdots}CH\overset{..}{\cdots}CH_2}} \quad (b)$$

it is clear that the allylic system in (*b*) is the more symmetrical and stable since the two C—C distances are more comparable in length. The product of reaction is indeed chloromethylallene[†] and not 1-methyl-3-chloroallene:

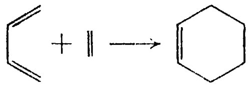
$$CH{\equiv}C{-}CH{=}CH_2 + HCl \rightarrow CH_2{=}C{=}CH{-}CH_2Cl$$

$$\textit{not}\ \ CHCl{=}C{=}CH{-}CH_3.$$

Terminal addition occurs in both phases of the reaction.

The Diels–Alder reaction

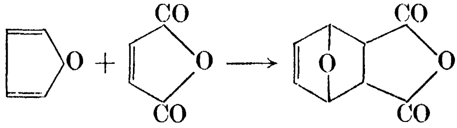
Conjugated dienes react with a variety of ethylene derivatives to give cyclohexenes, a reaction first investigated by Diels and Alder.

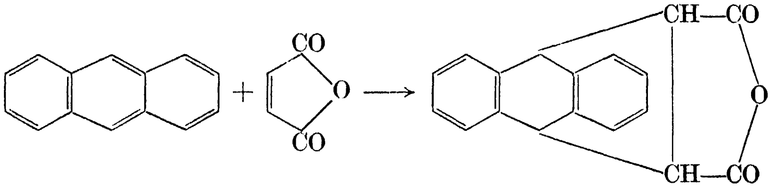


Since two double bonds in the starting material are replaced by four single bonds in the products, the heat of reaction should be approximately

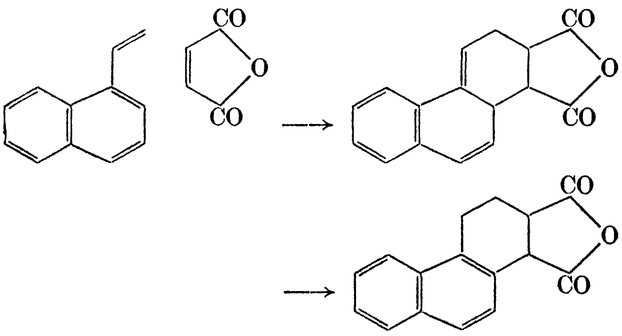
$$4E_{C-C} - 2E_{C=C} - R \simeq 30 \text{ cals.},$$

where R is the resonance energy of butadiene (*c.* 5 cals.). The reactions are usually very exothermic. So much energy is liberated that reaction can occur even if one of the reactants is aromatic; thus furane and anthracene will react readily with maleic anhydride.

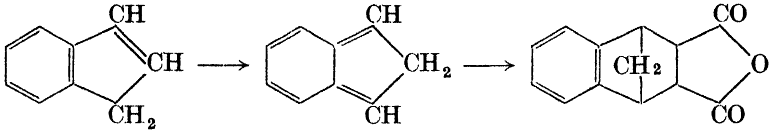




Similar reactions occur with 1-vinylnaphthalene and indene, the latter apparently reacting in a tautomeric form:

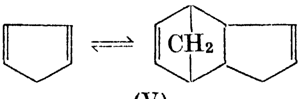


[†] Carothers and Berchet, *J.A.C.S.* **1933**, **55**, 2807.

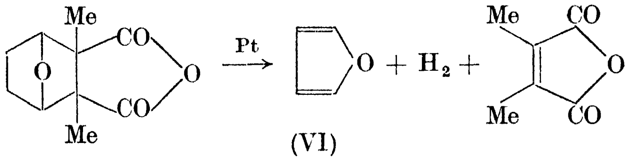


The more stable systems of benzene and thiophene do not, however, react.

The Diels–Alder reaction is reversible; thus cyclopentadiene forms its dimer (V) reversibly, while cantharidin (VI) is degraded by hot platinum into furane, hydrogen, and dimethylmaleic anhydride. (In the latter case the resynthesis from its components has not proved feasible.)



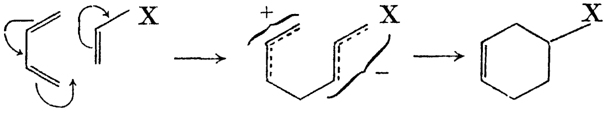
(V)



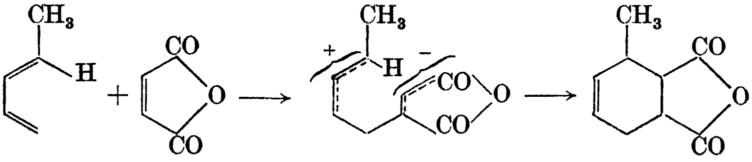
(VI)

Two different types of Diels–Alder reaction can be distinguished. The first occurs only if the olefinic component, or 'dienophil', has its double bond activated by a positive substituent (e.g. R·CO, CN, etc.) and takes place more readily in polar solvents; it must involve an ionic mechanism. The second type occurs between hydrocarbons and its rate is little affected by environment, being much the same in the gas phase as in solution; a radical mechanism seems likely.

In reactions of the first type it is reasonable to postulate anionoid attack by the diene on the cationoid dienophil; the product, a mesomeric zwitterion, then cyclizes.

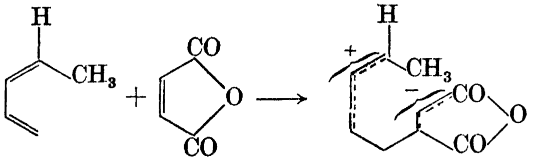


This mechanism is supported strongly by the work of Craig.[†] *Trans*-piperylene (VII) readily adds maleic anhydride to form a cyclic adduct, but *cis*-piperylene (VIII) gives only a polymer; apparently both forms give the same kind of intermediate zwitterion (IX), but that from *cis*-piperylene is prevented by steric hindrance from cyclizing.

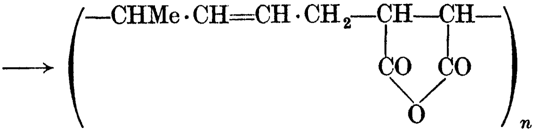


(VII) (IX)

[†] *J.A.C.S.* **1943**, **65**, 1006.

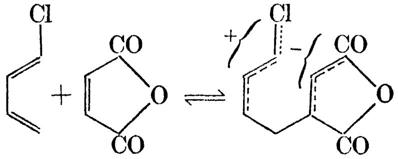


(VIII) (VII) (IX)

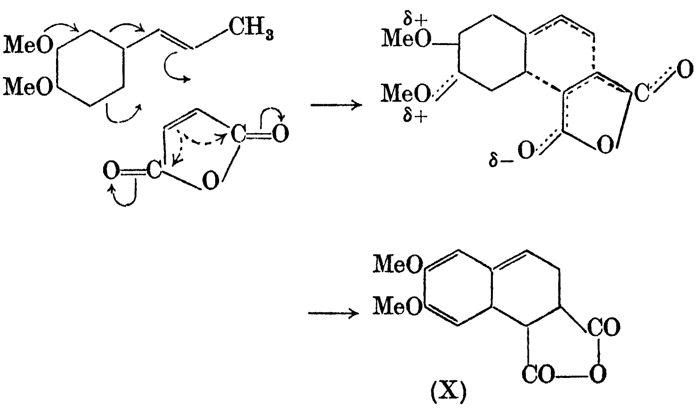


$$\xrightarrow{\quad}\left(\begin{array}{l}\text{—CHMe·CH=CH·CH}_2\text{—}\underset{\substack{|\\ \text{CO}}}{\text{CH}}\text{—}\underset{\substack{|\\ \text{CO}}}{\text{CH}}\text{—}\\ \qquad\qquad\qquad\qquad\qquad\qquad\quad \diagdown\;\diagup\\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{O}\end{array}\right)_n$$

The mechanism also explains why 1-chlorobutadiene will not react with dienophils;† apparently the —E chlorine stabilizes the intermediate carbonium system so effectively that neither ring-closure nor polymerization can occur; and since the formation of the intermediate zwitterion is presumably reversible, nothing but the starting material can be isolated.



Hudson and Robinson‡ have proposed an alternative mechanism for the addition of maleic anhydride to *iso*-eugenol and *iso*-saffrole. Such reactions with styrene derivatives occur only if both the 3 and 4 positions in the ring carry —E substituents and if the dienophil has +E substituents attached to both ends of the double bond. It seems likely, therefore, that the whole reaction takes place in one step:



(X)

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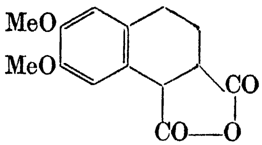
† Carothers et al., *J.A.C.S.* 1931, **53**, 4203; 1932, **54**, 4066; 1933, **55**, 2043.
‡ *J.C.S.* 1941, 715.

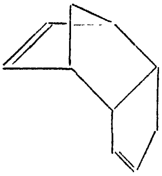


(XI)

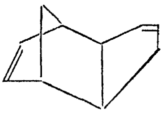
The product (X) then isomerizes to the benzene derivative (XI). This mechanism is certainly not general since singly and doubly activated dienophils usually react equally easily with dienes†; it is made necessary in this case by the great stability of the benzene ring.

The stereochemistry of the reaction

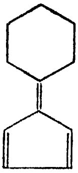
Alder and Stein‡ found that at low temperatures cyclopentadiene gave mainly the *endo* form (XII) of the dimer, but at high temperature more *exo* dimer (XIII) was formed. Similar effects have been observed by



(XII)



(XIII)



(XIV)

Woodward and Baer§ in the reaction between pentamethylenefulvene (XIV) and maleic anhydride. Wasserman‖ suggested some time ago that the diene and dienophil might form a molecular complex before reacting and that the stereochemistry of the complex might determine that of the adduct. The *endo* form of the complex will be the more stable since the polarizable groups in it will be in closer proximity (p. 184), and it will therefore be favoured at low temperatures. At higher temperatures the *exo* form is present in greater amount, the ratio of the two being $e^{\Delta F/RT}$ where ΔF is the free energy of interconversion. This theory has been restated without acknowledgement by Woodward,†† who, however, has adopted the erroneous views of Weiss concerning the nature of molecular complexes (p. 184).

The non-polar Diels–Alder reaction

Under drastic conditions, any diene will condense with any olefine; these reactions occur in the gas phase and so an ionic mechanism is out of the question. Two possibilities must be considered:† either the diene and dienophil first combine to a diradical which then cyclizes;

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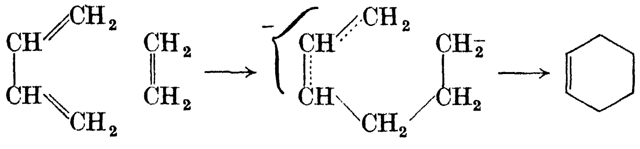
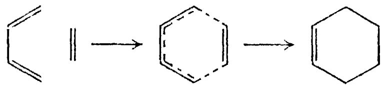
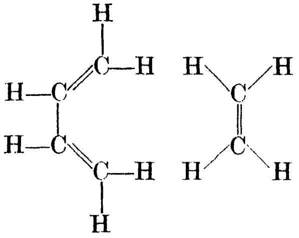
† Bergmann, Eschinazzi, and Neeman, *J. Org. Chem.* 1943, **8**, 179.
‡ *Annalen*, 1933, **504**, 219.
§ *J.A.C.S.* 1944, **66**, 645.
‖ *J.C.S.* 1935, 828, 1511; *Trans. Faraday Soc.* 1939, **35**, 841.
†† *J.A.C.S.* 1942, **64**, 3058.



or the two compounds combine by a single adiabatic process, the π-electrons in the transition state occupying six-atom orbitals analogous to those in benzene.



The latter mechanism, though attractive, is stereochemically improbable. If the π-orbitals are to overlap, they must be parallel and the whole system must be coplanar.



It is obvious that the terminal hydrogen atoms of the reactants will then interfere, and considerable distortion of bonds will be necessary before the carbon atoms can approach within bonding distance. Moreover, Kistiakowsky and Ransom‡ have measured the rate of dimerization of butadiene over a sufficient range of temperature for the frequency factor and activation energy to be determined. In this case the frequency factors for dimerization by the two mechanisms can be calculated by quantum mechanics (p. 29). The diradical mechanism would have a frequency factor of $0{\cdot}9\times10^{10}$, the cyclic mechanism one of about 10^{6}. The observed value, $1{\cdot}8\times10^{10}$, confirms the diradical mechanism. Moreover, the low activation energy (about 25 cals.) of dimerization of dienes is explained only by the radical mechanism. In the intermediate diradical there are two mesomeric allylic systems, each with a resonance energy of 15–20 Cals., while in the reaction with a normal olefine only one allylic system is present in the intermediate and the observed activation energies are much greater (about 40 cals.).

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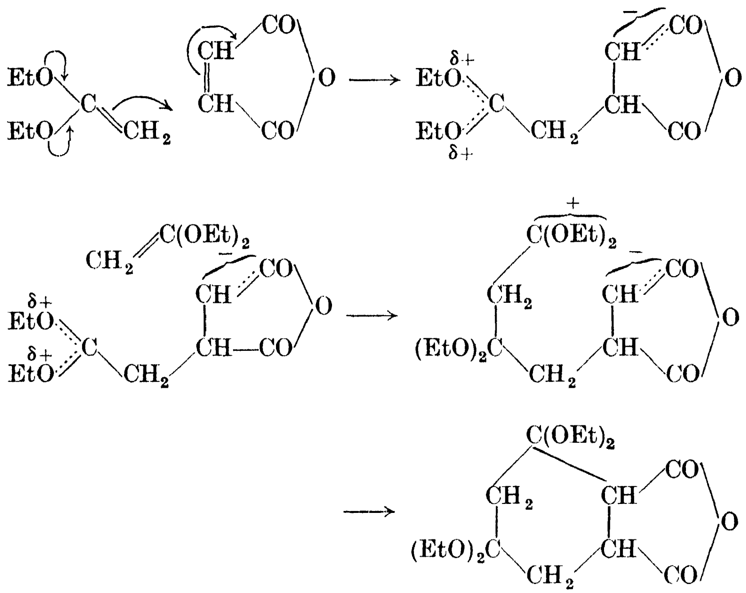
† Harkness, Kistiakowsky, and Mears, *J. Chem. Phys.* 1937, **5**, 682; Kistiakowsky and Ransom, ibid. 1939, **7**, 725.

‡ Ibid.

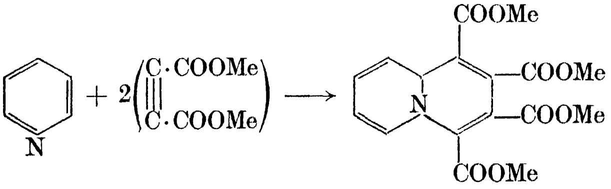
Other reactions of the Diels–Alder type

McElwain and Cohen† have recently found that ketene acetal will react with dienophils containing positive groups; the mechanism is presumably



and is completely analogous to the normal Diels–Alder reaction, two molecules of the strongly anionoid acetal replacing the diene.

Diels and Alder‡ have reported a similar reaction in which two molecules of methyl acetylenedicarboxylate replace the diene and pyridine the dienophil. Here the dienophil acts as the anionoid component.



(XV)

The resulting 'yellow compound' (XV), a lupinane derivative, gave α-picoline with strong alkali, confirming α-ring-closure. Diels§ was, however, able to isolate an intermediate 'red compound' which readily isomerized to (XV) on heating and in which ring-closure to the α-carbon had not occurred, since with strong alkali only pyridine, and oxalic and aconitic acids, were formed. Diels formulated the intermediate as

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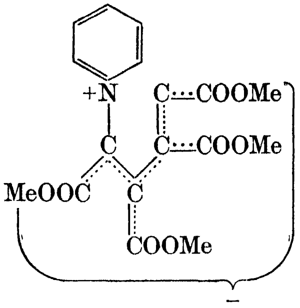
† *J.A.C.S.* 1942, **64**, 260.

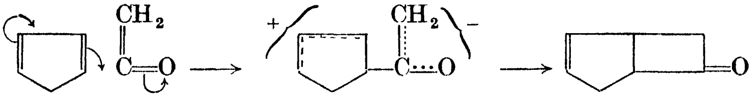
‡ *Annalen*, 1933, **505**, 103.

§ Ibid. 1934, **510**, 87; **513**, 129.

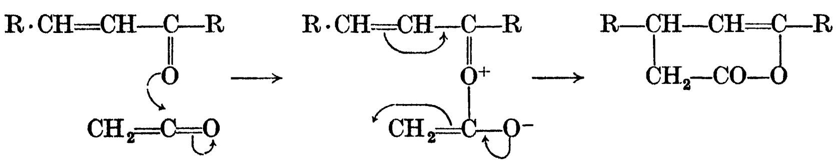


a structure exactly analogous to the zwitterionic intermediate postulated in the normal Diels–Alder mechanism. The stability of the intermediate in this case is not surprising since the isomerization to (XV) may require considerable activation energy, the 'red compound' being highly stabilized by mesomerism. Much of the resonance energy would be lost in the transition state for isomerization.

The reactions of ketene are worth mentioning; ketene generally undergoes 1:2 addition, cyclopentadiene, for example, giving 0:1:3-bicycloheptenone.†

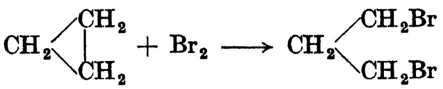


The 1:2 addition may be ascribed to a mutual polarization of the allylic and methylenecarbonyl systems in the intermediate. In normal Diels–Alder reactions the charged groups are farther apart and mutual polarization is smaller; the dominating effect is then the greater stability of 6-membered compared with 4-membered rings. If the intermediate is stabilized in any way, the greater ease of 6-ring formation may again control the ring-closure. This seems to be the case in the addition of ketene to α-β-unsaturated ketones whereby lactones are formed:



Cyclopropane derivatives

Cyclopropane can undergo cationoid addition reactions with halogens and hydrogen halides; e.g.



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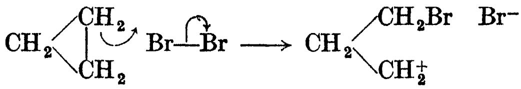
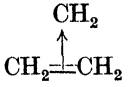
† Brooks and Wilbert, *J.A.C.S.* 1941, **63**, 870.

An obvious explanation would be that the reaction proceeds through an intermediate cation,

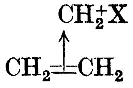


but the recent demonstration that the analogous olefine addition does not proceed through a simple carbonium ion intermediate suggests that the same is true here.

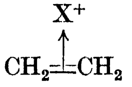
Calculation† by the molecular orbital method suggests that the asymmetrical π-complex (XVI) would have a binding energy comparable with that observed for cyclopropane; therefore whatever the actual electronic structure of cyclopropane itself may be,‡ we should expect it to combine readily with cationoid reagents to form π-complexes (XVII) closely analogous to the corresponding π-complexes (XVIII) from ethylene. The subsequent reactions of (XVII) and (XVIII) will be comparable, so we should expect the orientation of addition to be similar in substituted ethylenes and cyclopropanes. The most negative ring-carbon should add X^+ to form the π-complex, and the anion should then attack the most positive carbon. This orientation is observed.§


$$\begin{array}{c}CH_2\\ \uparrow\\ CH_2{=}CH_2\end{array}$$

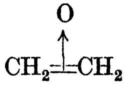
(XVI)


$$\begin{array}{c}CH_2^+X\\ \uparrow\\ CH_2{=}CH_2\end{array}$$

(XVII)


$$\begin{array}{c}X^+\\ \uparrow\\ CH_2{=}CH_2\end{array}$$

(XVIII)


$$\begin{array}{c}O\\ \uparrow\\ CH_2{=}CH_2\end{array}$$

(XIX)

Walsh‡ has also suggested that ethylene oxide has the π-complex structure (XIX), but as Robinson‡ has very forcibly pointed out, ethylene oxide bears no resemblance to amine oxides and so such a formulation is actively misleading. There is really no reason for abandoning the classical representations of cyclopropane and ethylene oxide; π-complex notation is useful only when no classical structures can be written. Thus in graphite oxide, the oxygen atoms are probably coordinated with the carbon layers to form coordinate molecular bonds, for it is sterically impossible that ethylene oxide structures should be present. It is likely that the peroxides of polynuclear aromatic hydrocarbons (e.g. coronene) have π-complex structures.||

Hyperconjugation; the alternation effect

When a series of methine groups are joined together into a conjugated (polyene) chain, their p-orbitals coalesce into a series of π-orbitals each

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† Dewar, *Trans. Faraday Soc.* 1948. Discussion on the Labile Molecule.

‡ Walsh (*Nature*, 1947, **159**, 165, 712) has suggested a kind of π-complex structure for cyclopropane; this has been criticized (Robinson, ibid. 1947, **159**, 400; **160**, 162; Sugden, ibid. **160**, 367; Coulson and Moffitt, *J. Chem. Phys.* 1947, **15**, 151; Dewar, loc. cit.), and the matter is still *sub judice*.

§ Kishner, *J. Russ. Phys. Chem. Soc.* 1912, **44**, 862; Davidson and Feldman, *J.A.C.S.* 1944, **66**, 488.

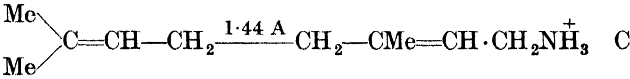
|| Cf. Coulson, *Trans. Faraday Soc.* 1946, **42**, 265.

extending over the whole conjugated system; but nevertheless the orders of the bonds in the chain fluctuate, so that the 1:2, 3:4, and 5:6 bonds in 1:3:5-hexatriene, for instance, have higher orders than the 2:3 or 4:5 bonds. This result follows at once from quantum-mechanical calculation of the bond-orders in such a system.

Now the mathematical treatment of such a conjugated polyene chain is precisely analogous[†] to the treatment of the hyperconjugated chain of methylenes in an *n*-paraffin. We should therefore expect a slight alternation of bond-orders in such chains, the effect being smaller than in a polyene since the overlapping of C—H orbitals in the former case (to form extended π-electron systems) is less efficient than the overlapping of *p*-orbitals in the latter (p. 19). The bond-lengths should therefore alternate slightly in *n*-paraffins.

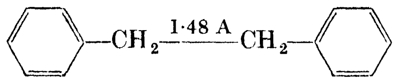
A larger effect would be expected in σ-bonds adjacent to π-bonds since the resulting first-order hyperconjugation is more important than the second-order hyperconjugation between σ-bonds. The effect should be particularly large in derivatives of diallyl and dibenzyl where a —C—C— group is sandwiched between two unsaturated systems.

Recently Jeffrey[‡] has established that the central bonds in two such compounds, geranylamine hydrochloride (XX) and dibenzyl (XXI), are abnormally short as the following figures show (normal C—C bond-length, 1·54 A).



$$\mathrm{Me_2C{=}CH{-}CH_2\overset{1\cdot 44\ A}{\text{———}}CH_2{-}CMe{=}CH{\cdot}CH_2\overset{+}{N}H_3\ \ \overset{-}{Cl}}$$

(XX) (max. error ±0·04 A)



(XXI) (max. error ±0·02 A)

The alternation effect in reaction rates

We may likewise expect an alternation in the effect of a substituent on the reactivity of an alkyl compound when the substituent is moved to carbon atoms successively more distant from the seat of reaction; just as a substituent in a benzene derivative produces different effects in the *o*-, *p*-, or *m*-positions. This effect is shown very clearly by the following table, where the relative rates of $-S_2$ replacement of a number of alkyl chlorides with potassium iodide in acetone are given. Positive substituents in the α- or γ-position accelerate reaction very greatly, while in the β-position their effect is much smaller and may even be in the opposite direction. The ω-phenylalkyl chlorides form a particularly interesting series since the alternation in rate, though small, is appreciable up to phenylheptyl chloride.

[†] Cf. Mulliken, Riecke, and Brown, *J.A.C.S.* 1941, **63**, 41.

[‡] Bateman and Jeffrey, *J.C.S.* 1945, 211; Jeffrey, *Proc. Roy. Soc.* 1947, **188** A, 222.

TABLE 21†

$Ph\cdot CO\cdot Cl$	2,220	$Ph\cdot CH_2\cdot Cl$	195
$PhCO\cdot CH_2Cl$	302,000	$Ph(CH_2)_2Cl$	1·12
$PhCO(CH_2)_2Cl$	86·7	$Ph(CH_2)_3Cl$	1·72
$PhCO(CH_2)_3$	372	$Ph(CH_2)_4Cl$	1·49
$AcO\cdot CH_2Cl$	270	$Ph(CH_2)_5Cl$	1·42
$AcO(CH_2)_2Cl$	0·45	$Ph(CH_2)_6Cl$	1·46
$AcO(CH_2)_3Cl$	39·5	$Ph(CH_2)_7Cl$	1·40
$Ph\cdot C{\equiv}C\cdot CH_2Cl$	782		
$PhC{\equiv}C(CH_2)_2Cl$	0·48		
$PhC{\equiv}C(CH_2)_3Cl$	1·9		

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† Conant and Kirner, *J.A.C.S.* 1924, **46**, 232; Conant, Kirner, and Hussey, ibid. 1925, **47**, 488; Murray, ibid. 1938, **60**, 2662. Rate-constants relative to butyl chloride at 50° except for the acetylenes (60°).

Effects on acid-strengths

A similar effect is observed in the dissociation constants of unsaturated acids. Acrylic acid is a much weaker acid than formic acid, because conjugation of the vinyl and carboxyl groups is more efficient in the parent acid than in its conjugate anion. The acid and anion both contain cross-conjugated systems in which the vinyl and hydroxyl (or O^-) compete to give electrons to the carbonyl; but the anionoid activity of O^- is so great that it wins easily in the anion, the vinyl perturbing the $—CO_2^-$ group very little, while the balance is much more even in the acid and so the perturbation there is greater. Hence the vinyl substituent increases the resonance energy of the acid more than it increases the resonance energy of the anion, and so it reduces the tendency of the acid to dissociate.

Now the effect of a C=C bond, when separated from a carboxyl by one or more methylene groups, should be transmitted to the carboxyl by hyperconjugation through the intermediate saturated chain, and from the considerations of the previous section, the transmission should be more efficient when an even number of carbon atoms separate the C=C and COOH groups. Therefore we should expect an alternation in acid-strength as successive carbon atoms are introduced between the two groups. This effect seems to occur (Table 22), though it is perhaps too small to be really significant.

TABLE 22

Acid	*pK*
$CH_3\cdot CH_2\cdot CH{=}CHCOOH$	4·69
$CH_3\cdot CH{=}CH\cdot CH_2\cdot COOH$	4·51
$CH_2{=}CH\cdot CH_2\cdot CH_2\cdot COOH$	4·68
$Ph\cdot COOH$	5·2
$Ph\cdot CH_2\cdot COOH$	4·3
$Ph\cdot CH_2\cdot CH_2\cdot COOH$	4·7

CHAPTER IX

AROMATIC COMPOUNDS

According to the current theory of aromatic properties, an aromatic compound may be defined as a cyclic compound with a large resonance energy where all the annular atoms take part in a single conjugated system. The general principles underlying this definition were discussed in Chapter I. From similar quantum-mechanical arguments it may be deduced that the conditions for a cyclic compound containing n atoms in the ring to be aromatic are:

(1) Each ring-atom must have a p-orbital available for π-bond formation, and the p-orbitals must be so oriented that they can all overlap to form large π-orbitals.

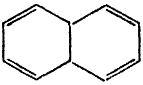
(2) The total number of electrons in the p-orbitals must be the even number, n or $(n+1)$.

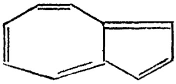
Aromatic compounds may be divided into two main groups: those with an even number of ring-atoms, each of which contributes one p-electron to the common stock, and those with an odd number of atoms where one ring-atom contributes two p-electrons. In the latter case, if the π-electrons are uniformly distributed round the ring, the share of each atom will be $(n+1)/n$ of an electron; thus the $(n-1)$ atoms which each contributed one p-electron will tend to gain a negative charge by virtue of the aromatic mesomerism, while the odd atom which contributed two p-electrons will become positively charged. This effect is well shown by pyrrole (cf. Chapter I).

These principles may be illustrated by a few examples.

1. *Naphthalene and azulene*

Both naphthalene (I*a*) and azulene (I*b*) satisfy the criteria for aromaticity, since each contains 10 ring-carbons each of which has a p-orbital suitably oriented for π-bond formation, and in both cases there are exactly 10 electrons to be fitted into the π-orbitals.

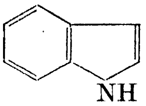

(I*a*)

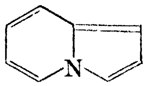

(I*b*)

Naphthalene is of course recognized as an aromatic compound, but there is little doubt that azulene is aromatic too, though its chemistry has been little studied on account of its inaccessibility. The resonance energy of azulene is less than that of naphthalene (p. 34), mainly because in it the valency angles of the carbon atoms are distorted from the 120° usual for sp_2 hybridization (p .7); but direct calculation also suggests that azulene should be somewhat the less stable (p. 36).

2. *Indole and indolizine*

These isomers both contain aromatic systems of the second type with 9 ring-atoms and $(9+1)$ π-electrons, of which the nitrogen contributes 2 in each case as in pyrrole.


(II*a*)


(II*b*)

Indole (II*a*) is well known to be aromatic; the aromatic nature of indolizine (II*b*) seems to have escaped notice. It is a typical aromatic nucleus as the properties recorded in Beilstein show. It undergoes nitration, halogenation, and acylation (Friedel–Craft) and, like indole, it is methylated in the nucleus by hot methyl iodide.

Reactions of aromatic compounds : Benzene

Although the classical (Kekulé) formula for benzene represents it as a triolefine, benzene does not usually give addition products. The reason for this is obvious; addition of, say, a halogen molecule would lead to a dihydrobenzene derivative which would no longer be aromatic; in this reaction the large resonance energy of benzene would be lost. Thus catalytic reduction of olefines to paraffins is a strongly exothermic reaction, but the corresponding reduction of benzene to dihydrobenzene is actually endothermic. Benzene therefore undergoes mainly substitution reactions, giving products which are still aromatic. In the majority of such reactions a cationoid reagent expels a proton from the ring, but similar substitution reactions are known where the reagent is anionoid or a radical. Only the ionic substitution reactions will be discussed here, radical substitutions being treated in Chapter XIII.

Cationoid substitution

The evidence that the usual substitution reactions of benzene involve cationoid attack may be summarized.

1. Halogenation is strongly catalysed by cationoid metal halides, a reaction best represented:

$$\mathrm{X{-}\overset{\curvearrowright}{X}\ AlX_3 \rightarrow X^+\quad X{-}\bar{A}lX_3}$$
$$\mathrm{X^+ + C_6H_6 \rightarrow C_6H_5X + H^+}.$$

That halogenation is an ionic process is shown by the greater rate of halogenation of phenols and phenol ethers in polar solvents.[†]

2. Iodination of benzene is catalysed by anhydrous silver perchlorate,[‡] indicating the mechanism

$$\mathrm{I_2 + Ag^+ \rightarrow I^+ + AgI}$$
$$\mathrm{I^+ + C_6H_6 \rightarrow C_6H_5I + H^+},$$

[†] Cf. Bradfield and Jones, *Trans. Faraday Soc.* 1941, **37**, 734.

[‡] Birkenback and Goubeau, *Ber.* 1932, **65**, 395, 1339; 1933, **66**, 1280; 1934, **67**, 917.

since Ag^+ ions are known to have a specific cationoid affinity for halogen. Moreover, iodination is readily effected by the brown solutions of iodine pentoxide and excess iodine in sulphuric acid,† which are believed for other reasons to contain the ions I_3^+ and I_5^+; while if the proportion of iodine is less, so that $(IO)^+$ ions are present, iodoxybenzene is formed.‡

3. Benzene is alkylated by secondary and tertiary alcohols in concentrated sulphuric acid; these solutions contain the alcohols as oxonium salts, which in the highly polar medium should readily give alkyl cations. Primary alcohols, where S_1 ionization should be much less facile, react less readily with benzene under these conditions, unless a —E substituent facilitates ionization (e.g. in $Ph \cdot CH_2OH$). Alkylation can also be effected by other reagents which can give alkyl cations (e.g. olefines with H_2SO_4 or HF; cf. p. 143). The Friedel–Craft reaction (p. 178) has also been shown to involve alkyl or acyl cations as intermediates.

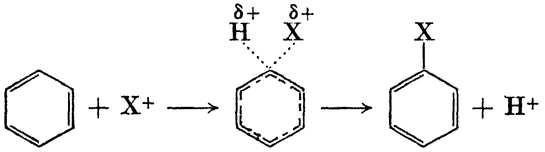
4. Nitration takes place readily in strong acids which can convert nitric acid into the reactive nitro cation:§

$$HO \cdot NO_2 + H^+ \rightarrow H_2O + NO_2^+.$$

This cation is formed in mixtures of nitric acid with concentrated sulphuric acid which are very powerful nitrating agents. In presence of water the less reactive cation $(H_2NO_3)^+$|| is formed, and nitration therefore occurs less readily. Perchloric acid is also a powerful nitration catalyst†† and is known to form a stable salt‡‡ with nitric acid where nitric acid acts as the base, and which is now§ known to be $(NO_2^+)(ClO_4^-)$.

Mechanism of substitution

Very few aromatic substitution reactions have been investigated kinetically, but in every case the rate has been found to depend on the concentration of the reagent. The reactions are therefore of $+S_2$ type and must pass through a transition state of the type:



In any case, a $+S_1$ mechanism is highly improbable since the unshared electrons in the ion $C_6H_5^-$ could not conjugate with the ring, the electrons occupying an atomic orbital at right angles to the π-orbitals of the ring. The ion would therefore not be stabilized relative to benzene, and its formation from benzene should be at least comparable in difficulty to the formation of an unstabilized alkyl anion from a paraffin.

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† Masson, *J.C.S.* 1938, 1708.

‡ Masson and Hanby, ibid. p. 1699.

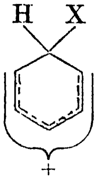
§ Ingold, et al., *Nature*, 1946, **158**, 480.

|| Halberstadt, Hughes, and Ingold, ibid. p. 514.

†† Müller, quoted by Robinson, *J.C.S.* 1941, 238.

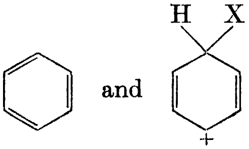
‡‡ Hantzsch, *Ber.* 1925, **58**, 958.

In the $+S_2$ transition state two of the original π-electrons are partially localized in the nascent bond with the reagent. The transition state therefore approximates to the structure



in which the remaining four π-electrons occupy the π-orbitals of a pentadienate cation. Of course the transition state does not actually have this structure since in it the replaced hydrogen and X will be attached to carbon by partial, not full, bonds, and the pentadienate system will conjugate with the electrons forming them (cf. $-S_2$ reactions of allyl halides, p. 73). However, the stability of the actual transition state probably runs parallel to the extreme form and no qualitative errors are introduced by identifying the two. Moreover, Wheland† has shown that substitution can be semi-quantitatively interpreted by quantum-mechanical calculations based on this approximation.

The ease of cationoid substitution in benzene, in contrast to its non-occurrence in unsubstituted paraffins, can be explained in such terms. The classical structures for benzene and the transition state,



differ in that the latter has one C—C π-bond less and one C—X bond more. The heats of formation of the two should therefore be comparable. And the resonance energy of benzene (36 Cals.) is not much greater than that of the pentadienate cation (26 Cals.). Hence the energy required to form such a transition state should be relatively small. In a paraffin, however, the analogous transition state

$$\overset{\delta+}{X}\cdots CR_3\cdots\overset{\delta+}{H}$$

would contain two weakened bonds and its energy of formation should be larger.

Effect of substituents

In the present approximation, conjugation of the rest of the ring with the replaced hydrogen and the replacing group is neglected in the transition state. Moreover, inductive effects will be small, since substituents cannot be directly attached to the carbon where replacement is taking place. Therefore the effect of substituents on the rate of reaction will be confined to changing the relative resonance energies of the initial and transition states, that is, relatively stabilizing or destabilizing the pentadienate cation in the latter.

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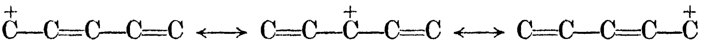
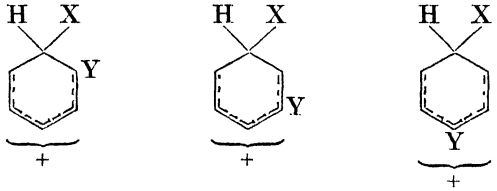
† *J.A.C.S.* 1942, 64, 900.

Following the general principles of Chapter IV, a —I-active substituent will stabilize a positively charged system more than an uncharged one, while a +I substituent will have the reverse effect. Hence a —I substituent will lower the energy required to convert benzene into the transition state for substitution and so accelerate reaction, while a +I substituent will conversely reduce the rate. Moreover, it can be shown by quantum-mechanical calculation (see p. 59), or by a consideration of the three main canonical forms of the pentadienate cation regarded as a resonance hybrid,



$$\overset{+}{C}{-}C{=}C{-}C{=}C \longleftrightarrow C{=}C{-}\overset{+}{C}{-}C{=}C \longleftrightarrow C{=}C{-}C{=}C{-}\overset{+}{C}$$

that the positive charge in such an ion resides on the 1-, 3-, and 5-carbon atoms. Hence writing the transition states for substitution of a benzene derivative, Ph—Y,



we see that the I-effect of Y will be greatest for substitution in the *o–p* positions. Therefore a —I substituent directs substitution mainly into the *o–p* positions, substitution occurring more readily than in benzene in all three positions; while a +I substituent lowers the rate of substitution all round the ring, but affects the *m*-positions less than the *o–p*; hence such a substituent seems to direct substitution into the *meta*-position, but in fact it acts by lowering the *o–p* reactivity even more than it does the *meta*.

The effect of E-substituents follows the same general principles. It can again be shown by calculation, or by writing resonance structures, that the π-orbitals of the pentadienate system conjugate most efficiently with an E-active substituent if the latter is attached to an odd-numbered carbon (see p. 59). A —E substituent will therefore stabilize the cation most effectively in the 1, 3, or 5 positions. Moreover, such a substituent will stabilize the cation more than it does the uncharged mesomeric system of benzene. Therefore —E substituents direct substitution strongly into the *o–p* positions. On the other hand, a +E substituent will not conjugate as effectively with the positive cation as with the uncharged starting material; such a substituent will therefore stabilize the latter more than the former and hence increase the energy, and lower the rate, of cationoid substitution.

Two further points require mention. Firstly, the common +E substituents 'direct' substitution mainly into the *meta*-position. A +E substituent should have little selective directing power since it will not conjugate appreciably with the pentadienate cation in the transition state. The *m*-direction can be ascribed to the powerful +I activity of all the usual +E substituents (NO_2, COOH, CN, CO·R, etc.) which leads to selective *o–p* deactivation. It is interesting in this connexion that the group—NMe_3^+ is more powerfully *m*-directing than any +E substituent,† even benzyltrimethylammonium salts (where the +I effect of nitrogen is buffered by an intermediate CH_2) substituting almost exclusively *meta*. And secondly, several substituents have opposed I- and E-effects, being +I—E (halogen, RO, R_2N). In these cases the E-effect is as usual the more important, and so substitution takes place *o–p*; but in the case of halogen the +I effect deactivates the whole ring so effectively that substitution in the *o–p* positions, though faster than in the *meta*, is still slower than in benzene.

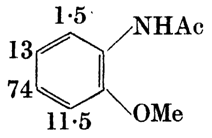
These conclusions are well illustrated by the relative rates of nitration of the various positions in several benzene derivatives, given in Table 23.‡

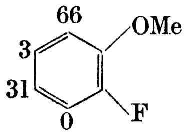
TABLE 23

	Ortho	*Meta*	*Para*	*Classification of* Y *in* PhY
Benzene	1	1	1	—
Toluene	43	3	55	−I−E
Ethyl benzoate	0·0026	0·0079	0·0009	+I+E
Chlorobenzene	0·03	0·000	0·139	+I−E
Bromobenzene	0·037	0·000	0·106	+I−E

Orientation in polysubstituted benzenes

The same principles apply. If both substituents in a disubstituted benzene have similar electronic properties, the more active directs substitution. Thus —E activity falls in the series NHAc > OMe > Cl; in benzene containing two of these groups *ortho* to one another, substitution will occur preferentially *o–p* to the more anionoid. The following results§ show that such is indeed the case. The figures indicate the percentage yields of the various mononitro derivatives formed on nitration.





Like substituents *meta* to one another will of course reinforce one another, so that *m*-dinitrobenzene reacts less readily than nitrobenzene in cationoid substitution and gives 1:3:5-trisubstituted benzenes, while resorcinol substitutes more readily than phenol and virtually exclusively in the positions *o–p* to the hydroxyls.

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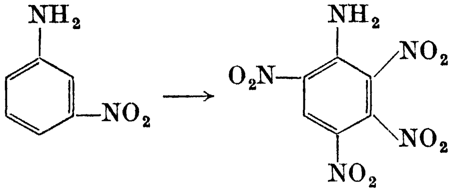
† Ingold, *Rec. trav. chim.* 1929, **48**, 797.

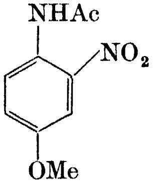
‡ Ingold et al., *J.C.S.* 1931, 1959; 1938, 905, 918.

§ Ingold and Ingold, ibid. 1926, 1310; Holmes and Ingold, ibid. p. 1328.

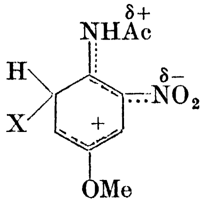
A special case of some interest arises when a +E and a −E substituent are both present. If they are *meta* to one another, the positive activating effect of the −E substituent wins and substitution occurs *o–p* to it; thus *m*-nitraniline gives tetranitraniline on nitration:



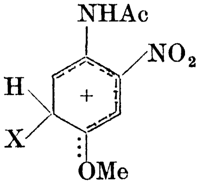
If the groups are *o* or *p* to one another, those forms of the quinonoid transition state will be stabilized the more strongly in which the groups can conjugate with one another. The effect is seen most clearly when a third substituent is present as is the case in *o*-nitroacetanisidide (III). In the three transition states for substitution (*a*), (*b*), and (*c*), such conjugation of the −E acetamido and +E nitro groups is possible only in (*a*) and (*c*). Also the positive charge on the ring is conjugated with methoxyl only in (*b*) and (*c*); hence (*c*) is the most stable of the three, and nitration therefore gives almost exclusively an *o*-dinitro derivative.



(III)



(*a*)



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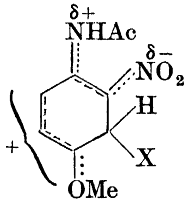
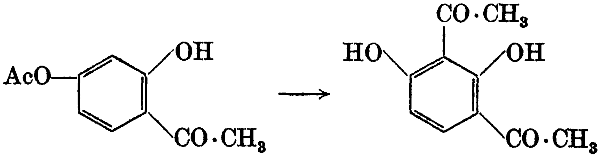


(*c*)

A similar example was reported by Baker†; Fries rearrangement of (IV), a reaction equivalent to acylation of the corresponding dihydroxyacetophenone by Ac^+, gives almost exclusively (V). Of the three possible transition states, (*c*) alone allows conjugation between *o*-hydroxyl and acetyl (with hydrogen bonding, p. 102) simultaneously with a stabilization of the annular charge by the other hydroxyl.



(IV) (V)

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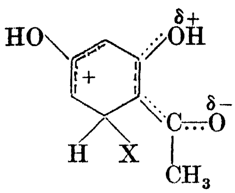
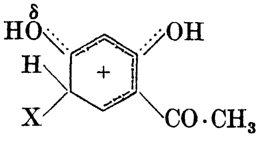
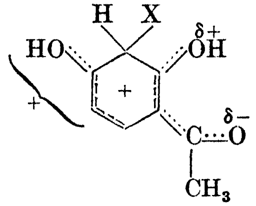
† Baker, *J.C.S.* 1934, 1684; Baker and Lothian, ibid. 1935, 628.



(*a*)



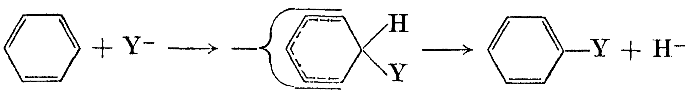
(*b*)



(*c*)

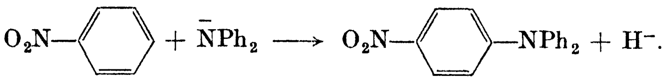
Anionoid substitution

Theoretically the anionoid substitution



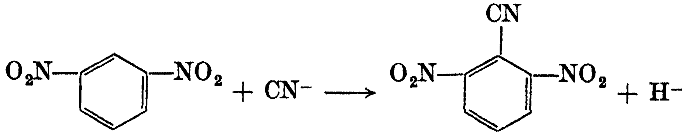
might be possible, but such reactions do not occur in benzene itself. The analogous replacement of more electronegative atoms is feasible, as in the hydrolysis of chlorobenzene to phenol by alkali at high temperatures, or the analogous hydrolysis of sodium benzenesulphonate to phenol by alkali fusion, but these reactions occur less readily than in the aliphatic series. Such reactions are $-S_2$ replacements in which the starting material has a larger resonance energy than the transition state. The unreactivity of chlorobenzene resembles that of vinyl chloride derivatives (p. 49).

If the pentadienate anion in the transition state is stabilized by appropriate $+E$ substitution, anionoid replacement occurs more readily. Thus the ease of $-S_2$ replacement of chlorine increases in the series chlorobenzene < *o*- or *p*-nitrochlorobenzene < 2:4-dinitrochlorobenzene < picryl chloride, the last-named compound reacting almost as readily as a carboxylic acid chloride. Indeed, even hydrogen may be replaced if such substituents are present; nitrobenzene will react with potassium diphenylimide to give 50 per cent. yields of N-(*p*-nitrophenyl) diphenylamine:†



The H^- ion presumably reduces some of the nitrobenzene and so the yield is not very high.

An analogous reaction is the conversion of *m*-dinitrobenzene to 2-methoxy-6-nitrobenzonitrile by cyanide ion in methanol; presumably anionoid replacement of hydrogen by CN^- is followed by anionoid replacement of one nitro-group by $\overline{MeO}$, the latter reaction being made possible by the strongly $+E$ CN group in the *ortho* position:



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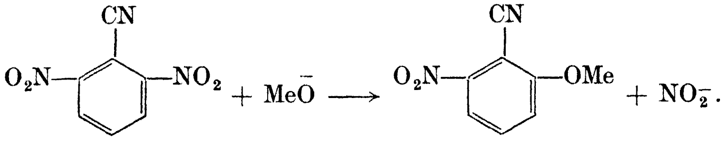
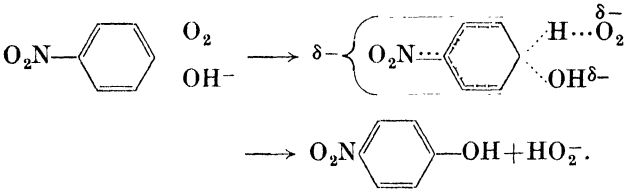
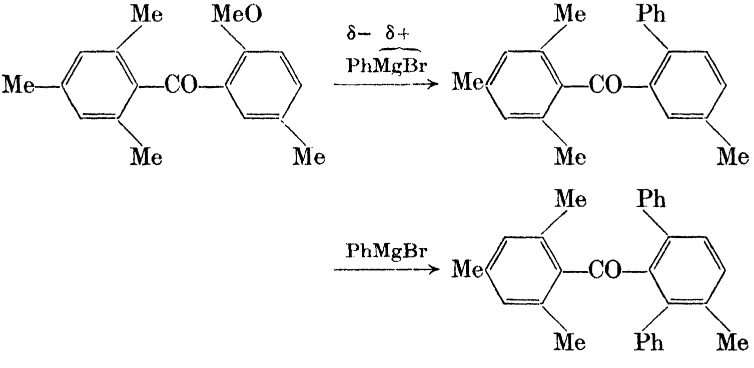
† Bergstrom, Granara, and Erickson, *J. Org. Chem.* 1942, **7**, 98.



It is interesting that these replacements of hydrogen in benzene only occur if nitro groups are present. This suggests that the replacement is really more complex, reaction occurring only if an oxidizing agent is present to react with H^- as it is formed. The conversion of nitrobenzene to *o*- and *p*-nitrophenols by air and hot potash, for instance, may involve a simultaneous attack by hydroxyl ion and oxygen:



Some very interesting anionoid substitutions by Grignard reagents have recently been described by Fuson and his collaborators.[†] In phenyl mesityl and phenyl duryl ketones, the carbonyl group is sterically hindered and will not react with phenyl magnesium bromide; but the benzene rings are activated to anionoid substitution by the $+$E carbonyl, and the Grignard reagent therefore attacks the ring. For example:

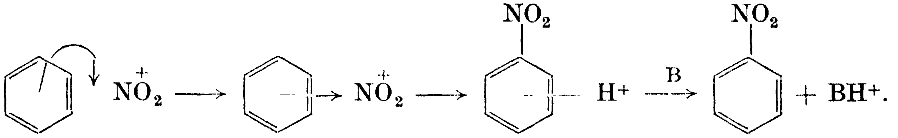


The first step is an anionoid replacement of methoxyl, the second a similar replacement of hydrogen. Both reactions take place in positions *ortho* to the carbonyl, as the general theory would lead us to expect.

π-Complex theory of cationoid substitution

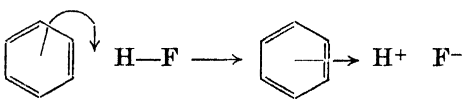
The reactions of olefines and benzene are closely parallel. Both react only with cationoid reagents unless specific ($+$E) activating groups are present. This rather suggests that the first step in cationoid substitution of benzene may be the formation of a π-complex with the reagent. The π-electrons of benzene should be well suited for dative bond-formation. The next step would then be a replacement of hydrogen in the ring to give a π-complex of H^+ and the product from which some base finally removes the proton. Thus nitration in sulphuric acid might be written:

[†] Fuson and Speck, *J.A.C.S.* 1942, **64**, 2446; Fuson and McKusick, ibid. 1943, **65**, 60; Fuson, McKusick, and Spangler, ibid. 1945, **67**, 597.



The actual replacement would involve a transition state of the same form as does the current mechanism, so the effects of substituents on orientation would be equally well explained; but the low activation energies of the reactions would be more easily intelligible, since in the replacement the replaced and replacing groups would be bonded before, during, and after reaction, so that the intermediates might well have relatively low energies. Indeed, the rate-determining step would probably be the initial formation of the π-complex. The rate of this step would be increased by negative substituents since these can confer a partial negative charge on the ring, lowering the ionization potential of the π-electrons and making them more available for dative bond-formation with the cationoid reagent, while positive substituents would conversely reduce the rate. Thus all the usual facts can be accounted for as well in terms of π-complex intermediates as in terms of direct S_2 replacement. This is of course no argument for the new theory, but several lines of evidence do seem to support its correctness.†

Firstly, there is good evidence that benzene can form stable π-complexes with protons. As far as is known, no substance dissolves in anhydrous hydrogen fluoride unless it is a salt or forms one with the solvent. Paraffins are therefore insoluble, and olefines are converted into alkyl cations with consequent polymerization (p. 284); but benzene and other aromatic hydrocarbons dissolve in anhydrous HF to give coloured solutions from which the hydrocarbon can be recovered unchanged by adding water or evaporating the solvent.‡ It seems almost certain that these solutions contain cations in which the hydrocarbon has acquired a proton and these cations can only be π-complexes; e.g.



Secondly, the very high dipole moment (5 D) of aluminium bromide in dilute benzene solution† must imply coordination with the solvent, a result only explicable if a π-complex is formed:

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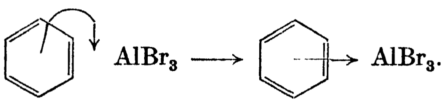
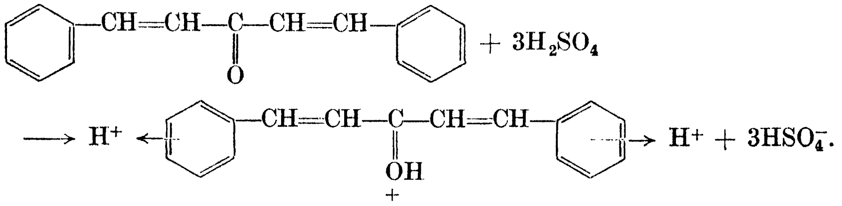
† Incidentally, the π-complex interpretation avoids an awkward inconsistency. The explanation for the ease of cationoid substitution (p. 163) should apply equally to anionoid substitution, and the explanation for the difficulty of anionoid substitution (p. 167) to cationoid substitution!

‡ Klatt, *Z. anorg. Chem.* 1937, **234**, 189.

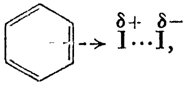


In more concentrated solution, or in CS_2, the halide is present mainly in a non-polar dimeric form.

Thirdly, Hammett and Deyrup‡ have found that solutions of dibenzylideneacetone in concentrated sulphuric acid show a four-fold depression of freezing-point, a result which shows clearly that each molecule of ketone binds three protons; one is of course attached to the basic oxygen of the carbonyl group, but the other two must be held by π-electrons:



The abnormal colour and dipole moment (~ 1 D) of iodine solutions in benzene may possibly be due to partial π-bond formation,



and the photoxides of anthracene derivatives may have a similar structure (p. 157).

Fourthly, there is definite evidence that a *m*-methoxy group increases the rate of cationoid substitution in benzene, although in the *m*-position its —E action will not operate and it should behave as a +I substituent and lower the rate of substitution. (In side-chain reactions *m*-methoxyl does indeed act as a positive substituent, p. 173.) A simple example is the ready nitration of veratrole by cold dilute nitric acid, under conditions where anisole is scarcely attacked.§ According to the π-complex theory, the rate of substitution is determined by the net anionoid reactivity of the ring and not by the reactivity of individual positions in it; a —E methoxyl in any position will increase the electron density of the ring as a whole and so facilitate cationoid substitution.

Fifthly, while aniline and phenol normally substitute both *ortho* and *para*, they couple exclusively *para* with diazonium salts. The reactions therefore probably involve a different mechanism. Now the ease of formation of the π-complex will depend on the reactivity of the cationoid reagent. Most substituting agents, Br^+, NO_2^+, alkyl$^+$, acyl$^+$, etc., are extremely reactive electron-deficient cations which are only exceptionally observed in the free state; but benzenediazonium cations are quite stable, and indeed their classical formulae imply that they contain no empty orbitals (e.g. $Ph-\overset{+}{N}\equiv N$). Therefore the latter should have little tendency to form π-complexes, and coupling (p. 182) probably occurs by a classical S_2 mechanism. Like anionoid replacement in benzene, this direct replacement is made possible only by appropriate substituents in the ring (here $-E$ substituents such as NH_2, O^-). Coupling would therefore be the cationoid counterpart of the anionoid substitutions discussed in the last section. This suggestion would also account for the different course of coupling to normal substitution. In coupling, the replacement reaction determines the rate; its activation energy will be relatively high, and small fractional differences in activation energy for *o*- and *p*-reaction will produce a considerable difference in the absolute activation energies, and so in the relative rates of *ortho* and *para* coupling. In the π-complex mechanism, the actual replacement is a rapid reaction with, presumably, a low activation energy; corresponding fractional differences will mean a much smaller absolute difference in activation energy for *ortho* and *para* substitution, and so we might anticipate that more equal proportions of the isomers would be formed.

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† Nespital, *Z. phys. Chem.* 1932, B **16**, 153.

‡ *J.A.C.S.* 1933, **55**, 1900. A dihydrobromide of dibenzylideneacetone and a dihydrochloride of dicinnamylideneacetone have actually been isolated (Vorländer and Hayakawa, *Ber.* 1903, **36**, 3537; Stobbe and Haertel, *Annalen*, 1909, **370**, 101).

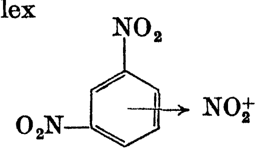
§ Cardwell and Robinson, *J.C.S.* 1915, **107**, 256.

Sixthly, a number of typical cationoid substitution reactions of benzene take place with simultaneous migration of substituents in the ring. It seems impossible to explain these rearrangements satisfactorily except in terms of π-complex intermediates (pp. 231, 233). There is therefore clear evidence that in these cases, at least, π-complexes are involved in typical aromatic substitutions.

And finally, Bennett and his collaborators have found† that the nitration of dinitrotoluene in sulphuric acid follows the third-order rate-law

$$\frac{d[\mathrm{TNT}]}{dt} = k\{a[\mathrm{HSO_4^-}]+b[\mathrm{HS_2O_7^-}]+c[\mathrm{H_2SO_4}]\}[\mathrm{DNT}][\mathrm{NO_2^+}].$$

Now it is extremely improbable that the reaction is truly termolecular, since hardly any examples of true termolecular reactions are known. It is much more likely that two of the reactants combine rapidly and reversibly to form an intermediate, which then reacts relatively slowly with the third reactant (see p. 21 for an appropriate kinetic analysis). If this is in fact so, the intermediate is not easy to formulate in classical terms; but we should expect the π-complex



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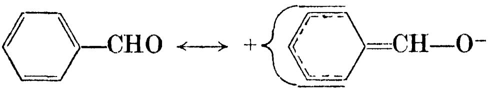
† Bennett, Brand, James, Saunders, and Williams, ibid. 1947, 474.

to have the requisite properties, since in this case the ring is deactivated by the nitro groups. Not only will the stability of the π-complex thus be lowered, but also its conversion to the normal substitution product may well require a base to take up the proton (HSO_3^-, $HS_2O_7^-$, and H_2SO_4 are bases in the sulphuric acid system, just as HO^- and H_2O are bases in the water system).

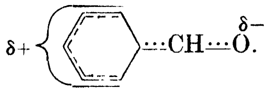
In the rest of the chapter we shall omit the π-complex details of substitution for clarity and brevity, but it is likely that all normal cationoid substitution in aromatic compounds involves the initial formation of π-complexes with the reagents.†

Side-chain reactions

Phenyl can act as a +E or −E substituent in other molecules. When it does so, the resulting state may be written as a mesomer between classical and quinonoid forms; for example, benzaldehyde may be written



or more simply as



The E-effect of the phenyl will be increased by substituents which stabilize the charge on the nucleus; and since the mesomeric state of the phenyl resembles that in the quinonoid transition state for substitution, it follows that a positive charge will be stabilized strongly by −E substituents in the *o–p* positions, less by −I substituents in the *o–p* positions, and less again by −I substituents in the *m*-positions; a negative charge being stabilized similarly by the corresponding positive substituents. Moreover, a positive charge will be destabilized by positive substituents, +I being more active in the *o–p* positions, and a negative charge will be correspondingly destabilized by negative substituents. The inactivity of E-substituents in the *meta*-position can be deduced from the rule given by Coulson and Longuet-Higgins, p. 59.

In a reaction of a benzene side-chain where the rate is affected by the E-effect of phenyl, substituents will affect its E-activity and so alter the rate of reaction. Thus benzaldehyde is less reactive than aliphatic aldehydes to anionoid reagents since in it the benzene ring (here −E) conjugates with the carbonyl. This conjugation is greater in benzaldehyde derivatives with negative substituents, less with positive substituents. Therefore anisaldehyde, for example, reacts less readily, *p*-nitrobenzaldehyde more readily, than benzaldehyde with anionoid reagents.

Hammett‡ has shown that in a large variety of such side-chain reactions the effect of *m*- and *p*-substituents on the rate can be expressed in a simple quantitative form. If k_0 is the rate constant of reaction for the unsubstituted compound, k for the substituted compound, then for many reactions

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† This conclusion is further supported by quantum-mechanical calculations by Dewar, *Faraday Society Discussion on the Labile Molecule*, 1947.

‡ *J.A.C.S.* 1937, **59**, 96.

$$\log k - \log k_0 = \rho\sigma,$$

where ρ is constant for any one reaction and σ for any one substituent in different reactions. The greater $\rho\sigma$, the greater the increase in rate due to the substituent; so the numerical value of σ indicates the quantitative effect of a given substituent on the reaction rate. Some values of σ are given in Table 24.

TABLE 24

Substituent	σ
p-NH$_2$	−0·660
p-OMe	−0·268
p-Me	−0·170
p-Et	−0·144
p-Pr$_\beta$	−0·151
p-Bu$_\gamma$	−0·197
m-Me	−0·069
p-F	+0·062
m-OMe	+0·115
p-Cl	+0·227
p-Br	+0·232
p-I	+0·276
m-Cl	+0·373
m-COOH	+0·355
m-NO$_2$	+0·710
p-COOH	+0·728
p-NO$_2$	+0·778†

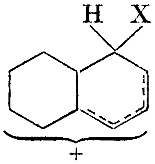
† For aniline and phenol derivatives a higher value (+1·27) is found.

These results are of great interest. Firstly, they are in exact accord with the qualitative predications of the electronic theory. We use the same convention of signs as does Hammett so that comparison is simplified. The positive effect of *m*-methoxyl is particularly striking and we have already referred to it in another connexion (p. 170). The greater cationoid activity of halogen in the *m*-, and of COOH and NO$_2$ in the *para*-position, is of course to be expected. The effect of *p*-alkyl substituents is most interesting. The −E effect, due to hyperconjugation, falls in the series Me $>$ Et $>$ Pr$_\beta$ $>$ Bu$_\gamma$, while the −I effect rises in the same order. The combination of two effects leads to a minimum in net anionoid activity between ethyl and *iso*-propyl. Incidentally the −E and +I effects of halogen both fall in the series F $>$ Cl $>$ Br $>$ I, and it is interesting that in the *p*-position the E-effect evidently predominates (as we have assumed previously), since the net anionoid activity falls in the same order.

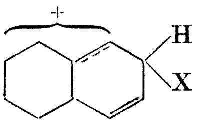
Naphthalene

In reactions which convert benzene into non-aromatic products, the resonance energy of benzene (36 Cals.) is lost. On the other hand, in reactions which convert naphthalene to tetralin derivatives, only the smaller difference (27 Cals.) between the resonance energies of naphthalene and benzene is lost. Therefore naphthalene is less aromatic than benzene and can, for example, be reduced more easily to tetralin than can benzene to cyclohexane.

The substitution reactions of naphthalene generally resemble those of benzene, with some important differences. Naphthalene unlike benzene can give two monosubstitution products. We may write the corresponding transition states formally as



(α)



(β)

Of course the actual transition states only approximate to these quinonoid structures, but they resemble them qualitatively and (as in benzene) we may conveniently discuss substitution in terms of them. Now the (α) state contains a phenylallyl cation, the (β) state a benzyl cation; our general principles suggest that the former should be the more stable, since it contains a larger conjugated system.† Naphthalene does indeed substitute mainly α at moderate temperatures. It is interesting that at high temperatures β-substitution predominates, a fact which makes possible the technical production of β-naphthalenesulphonic acid, and hence of other β-naphthyl derivatives. The most reasonable explanation seems to be that the entropy of activation is greater for β- than for α-substitution, since α-substitution is sterically hindered by the *peri*-CH, while the activation energy for β-substitution is also the greater. Therefore the rates of substitution are given by

$$A_\alpha e^{-E_\alpha/RT} \quad \text{and} \quad A_\beta e^{-E_\beta/RT},$$

where $A_\beta > A_\alpha$ and $E_\beta > E_\alpha$. At low temperature $e^{-E_\alpha/RT} \gg e^{-E_\beta/RT}$ and so α-substitution predominates, but at higher temperatures, when the ratio of the exponential terms is smaller, the rate of β-substitution becomes the greater.

The further substitution of monosubstituted naphthalenes is also rather complex. In the benzyl and phenylallyl cations forming the transition states, the charge is concentrated mainly in the side-chain, so that substitution will affect their stability more if the substituent is in the side-chain than if it is in the nucleus. Also it may be shown (see p. 164) either by quantum-mechanical calculation, or by writing resonance forms, that substituents will have most effect in the *o*- and *p*-positions of the phenyl, and in the 1- and 3-positions in the side-chain of (phenylallyl)$^+$. A negative substituent in the α-position will therefore direct substitution mainly into the 2- and 4-positions, and will activate less strongly the 5- and 7-positions in the other ring.

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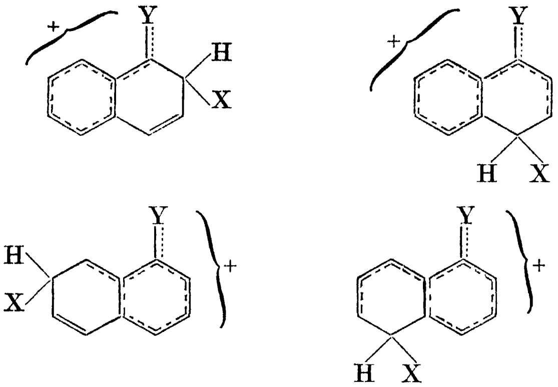
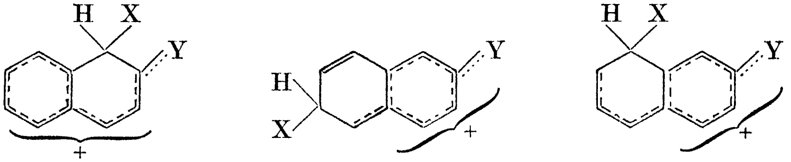
† The resonance energies may be calculated by quantum mechanics to be: $\mathrm{PhCH_2^+}$, 52 Cals.; $(\mathrm{Ph{\cdots}CH{\cdots}CH{\cdots}CH_2})^+$, 61 Cals.

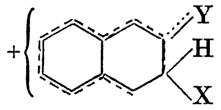


Since substitution in the 7-position involves a transition state resembling a benzyl cation, and in the 5-position one resembling a phenylallyl cation, substitution, if it occurs in the other ring, takes place preferentially in the 5-position.

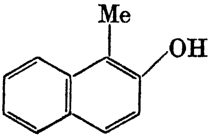
A negative β-substituent activates the adjacent α-position strongly and the 6- and 8-positions weakly:



Such a substituent will not activate the adjacent β-position at all, since in the corresponding quinonoid transition state the second benzene ring would not be aromatic; the substituted octatetraenyl cation would have a much smaller resonance energy than a benzyl or phenylallyl cation.

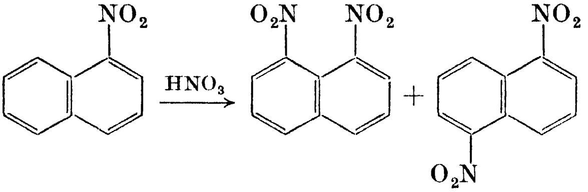


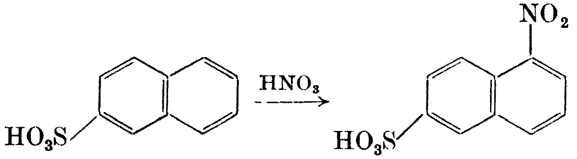
It is, of course, well known that negative substituents in the α-position of naphthalene do direct further substitution primarily into the 2- and 4-positions, while β-substituents activate the adjacent α-position strongly but do not activate the adjacent β-position at all (e.g. 1-methyl-2-naphthol,



will not couple in the 3-position under any conditions).

Conversely, the deactivating effect of a positive substituent will be greatest in its own ring; such compounds, e.g. α- or β-nitronaphthalene, substitute in the other ring, and give α-substitution products for the same reason that does naphthalene itself. Moreover, an α-substituent will deactivate the 5- and 7-positions in the other ring more strongly than the 6- and 8-positions and a β-substituent will have the opposite effect. It is, indeed, found that nitration of α-nitronaphthalene gives amounts of 1:8-dinitronaphthalene which are remarkably large when one considers the steric hindrance that must arise between the *peri*-nitro groups; while naphthalene-β-sulphonic acid on nitration gives mainly 1-nitronaphthalene-6-sulphonic acid.





Anionoid substitution in naphthalene

Cationoid substitution in naphthalene probably occurs by a π-complex mechanism as in benzene, but anionoid substitution must again take place by a direct S_2 replacement through a transition state of the usual quinonoid type. Although the transition states only approximate to the extreme forms we have been writing, it is reasonable to suppose that their energies are roughly proportional to those of our quinonoid structures. We may then get a rough idea of the relative activation energies for anionoid replacement in different ring systems from the difference in the resonance energies of the initial and quinonoid transition states. These may be calculated very simply by approximate quantum-mechanical methods. The results for substitution in benzene and in the α- and β-positions of naphthalene are given below (p. 177).

Naphthalene may therefore be expected to undergo anionoid substitution more readily than benzene, substitution taking place in the α-position. Naphthalene does indeed differ from benzene in that the parent hydrocarbon can be substituted by certain anionoid reagents. Thus with sodamide it gives α-naphthylamine and 1:5-diaminonaphthalene.†

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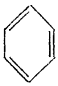
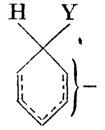
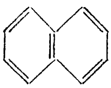
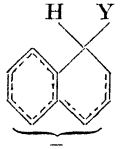
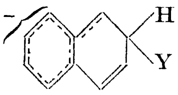
† Sachs, *Ber.* 1906, 39, 3006.

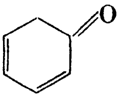
Parent compound	*Resonance energy*	*Transition state*	*Resonance energy*	*Difference in resonance energy*
	36 Cals.		26 Cals.	10 Cals.
	63 ,,		61 ,,	2 ,,
,,	63 ,,		52 ,,	11 ,,

Other aromatic hydrocarbons

Little would be gained by a detailed survey of substitution in polynuclear hydrocarbons since no new principles are involved. For instance, anthracene is less aromatic than naphthalene, and substitutes most readily in the 9-position. These results can be immediately explained. The difference in resonance energy between anthracene and dihydroanthracene is small (16 Cals.) in contrast to the larger difference between naphthalene and tetralin (27 Cals.); therefore anthracene is much more easily reduced than naphthalene and it gives exclusively 9:10-dihydroanthracene since this has a much larger resonance energy (72 Cals.) than 1:2:3:4-tetrahydroanthracene (63 Cals.). The ready 9-substitution follows from the analogous fact that the diphenylmethyl cation has a much larger resonance energy than any naphthylmethyl or naphthylallyl cation.

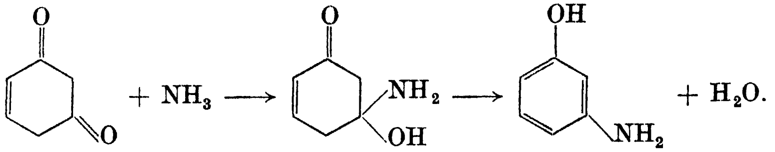
Keto-enol tautomerism in the aromatic series

Normally the ketonic form of a ketone is much more stable than the enol because the sum of the C═O and C—C bond-energies in the ketone is greater than the sum of the C—O and C═C bond-energies in the enol; but in aromatic compounds containing hydroxyl groups the corresponding ketonic tautomers are not aromatic, and are therefore destabilized to the extent of the resonance energy of the phenol. Thus phenol itself has no tendency to react in the ketonic form.

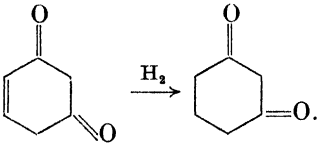


However, if a second hydroxyl group is introduced into benzene the difference in energy between classical structures for the diketone and dienol forms becomes so great that some ketonic reactions may be observed.

Thus resorcinol reacts quite readily with ammonia to give *m*-aminophenol, *a reaction best represented as a carbonyl addition of the ketonic form:*



Moreover, resorcinol very readily gives dihydroresorcinol on reduction:



In phloroglucinol, where three hydroxyl groups are present, ketonic properties become marked, and this compound may even be appreciably tautomeric. Addition of an *o*-hydroxyl to a phenol does not increase its ketonic tendencies, since the diketo form would be a cyclic 1:2-diketone and such compounds are destabilized by mutual repulsion of the C=O dipoles (p. 102).

In less aromatic ring-systems even monophenols may show ketonic reactions. Thus in converting naphthol to the corresponding ketonic tautomer, only the difference in resonance energy between naphthalene and benzene is lost, and in the case of 9-hydroxyanthracene, the still smaller difference between anthracene and 9:10-dihydroanthracene. Naphthols are readily converted to naphthylamines by ammonium sulphite (Bucherer reaction), while the enol and keto forms of 9-hydroxyanthracene are of comparable stability.

Friedel–Craft reaction

Alkyl and acyl halides will react with aromatic hydrocarbons in presence of strongly cationoid metal halides, especially aluminium chloride, to give alkyl or acyl derivatives of the hydrocarbon. From the orientation and ease of formation of the products in the analogous reactions of substituted benzenes, it is certain that the reactions are cationoid substitutions; and it has been established that the actual reagents are alkyl or acyl cations formed by cationoid attack on the halide by the catalyst, e.g.

$$\mathrm{AcCl} + \mathrm{AlCl_3} \rightarrow \mathrm{Ac^+} \quad \mathrm{AlCl_4^-}$$

$$\mathrm{PhH} + \mathrm{Ac^+} \rightarrow \mathrm{Ph\cdot Ac} + \mathrm{H^+}.$$

The evidence may be summarized.

1. Aluminium chloride gives complexes with alkyl and acyl halides which conduct electricity and must therefore be salts. A detailed investigation by conductivity measurements led Wertyporoch and his collaborators†

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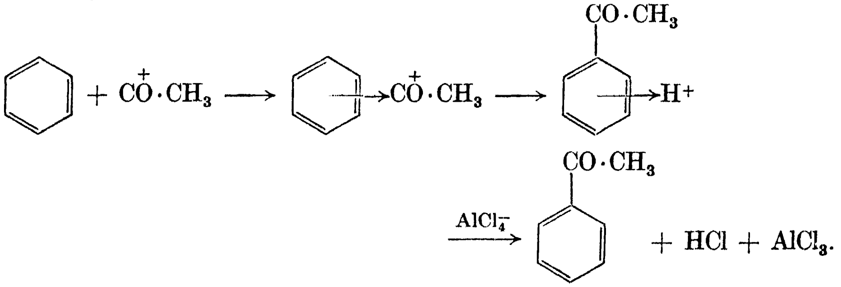
† *Ber.* 1931, **64**, 1357, 1369; *Z. phys. Chem.* 1932, **162**, 398; *Annalen*, 1933, **500**, 287.

to the conclusion that the complex so formed combines with the aromatic hydrocarbon to give a still more strongly conducting ternary complex, the latter then breaking down into the products.

$$\mathrm{RCl} + \mathrm{AlCl_3} \rightarrow \mathrm{R^+} + \mathrm{AlCl_4^-}$$
$$\mathrm{R^+} + \mathrm{ArH} \rightarrow (\mathrm{ArH, R})^+$$
$$(\mathrm{ArH, R})^+ + \mathrm{AlCl_4^-} \rightarrow \mathrm{Ar{-}R} + \mathrm{HCl} + \mathrm{AlCl_3}.$$

Not only does this work establish the general mechanism of the reaction but it also provides good evidence for the π-complex theory of substitution. The cation $(\mathrm{ArH, R})^+$ must be a π-complex. Thus the acetophenone synthesis may be written


$+ \overset{+}{\mathrm{C}}\mathrm{O \cdot CH_3}$
$\overset{+}{\mathrm{C}}\mathrm{O \cdot CH_3}$
$\mathrm{CO \cdot CH_3}$
$\mathrm{H^+}$
$\mathrm{CO \cdot CH_3}$
$\mathrm{AlCl_4^-}$
$+ \mathrm{HCl} + \mathrm{AlCl_3}.$

2. Fairbrother† has shown that when benzene reacts with *tert*-butyl or acetyl chloride in presence of aluminium chloride containing radioactive chlorine, the chlorine in the evolved hydrogen chloride contains exactly 75 per cent. as much radiochlorine as did that in the original $\mathrm{AlCl_3}$. Complete exchange of chlorine atoms must therefore occur during reaction, a result suggesting strongly that some symmetrical intermediate such as $\mathrm{AlCl_4^-}$ is involved.

A number of reactions are known which resemble the Friedel–Craft reaction in that the reagent is a carbonium ion. The carbonium ion may be formed either by $\mathrm{S_1}$ ionization of an oxonium salt, or by addition of a proton or other cationoid reagent to the double-bond of an olefine. Thus aromatic compounds react with alcohols in strong sulphuric acid:

$$\mathrm{ROH} + \mathrm{H_2SO_4} \rightarrow \mathrm{RO\overset{+}{H}_2} + \mathrm{HSO_4^-}$$
$$\mathrm{ROH_2^+} \rightarrow \mathrm{R^+} + \mathrm{OH_2}$$
$$\mathrm{R^+} + \mathrm{PhH} \rightarrow \mathrm{PhR} + \mathrm{H^+}.$$

The reaction occurs most readily with tertiary alcohols, less so with secondary; and rarely with primary unless the ionization is facilitated either by a $-\mathrm{E}$ substituent (e.g. $\mathrm{PhCH_2OH}$) or by a possibility of rearrangement to a more stable cation (e.g. $\mathrm{Me_2CH \cdot CH_2OH}$; *vide* p. 208). In these cases there is independent evidence for $\mathrm{S_1}$ ionization in sulphuric acid. Anhydrous HF and $\mathrm{BF_3}$ bring about similar condensations. Acids, esters, etc., may also react, possibly by $+\mathrm{S_1}$ ionization to an acyl cation

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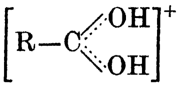
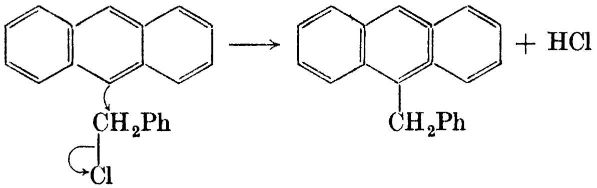
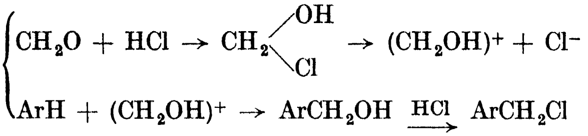
† *J.C.S.* 1937, 503; see also *Trans. Faraday Soc.* 1941, 37, 763.

(p. 122), possibly by reaction of the aromatic compound with a highly cationoid salt such as  $\left[R-C\begin{smallmatrix}\cdot OH\\ \cdot OH\end{smallmatrix}\right]^+$. (In this connexion it is likely that the uncatalysed reaction of benzyl chloride with anthracene proceeds by a $-S_2$ replacement of chlorine by the strongly anionoid hydrocarbon.

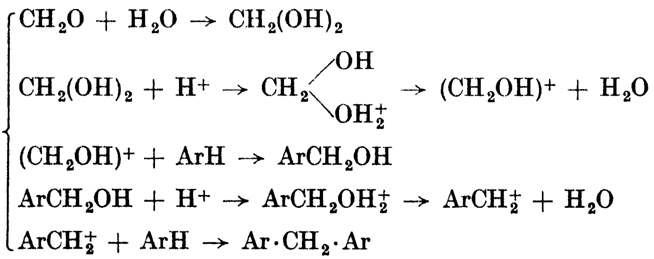


An intermediate ionization of the halide is unlikely since less reactive aromatic compounds (e.g. benzene) do not condense with benzyl chloride although they react readily with the benzyl cation formed from the chloride and $AlCl_3$.)

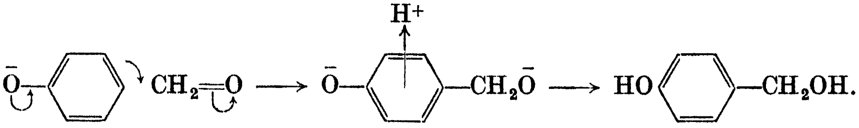
Other reactions of the same type are the chloromethylation of hydrocarbons by formaldehyde in presence of HCl, their condensation with formaldehyde in sulphuric acid to diphenylmethane derivatives, and the hydroxymethylation of phenols by formaldehyde and alkali. It will suffice to give equations:



$$\begin{cases} CH_2O + HCl \rightarrow CH_2\begin{smallmatrix}OH\\ Cl\end{smallmatrix} \rightarrow (CH_2OH)^+ + Cl^- \\ ArH + (CH_2OH)^+ \rightarrow ArCH_2OH \xrightarrow{HCl} ArCH_2Cl \end{cases}$$



$$\begin{cases} CH_2O + H_2O \rightarrow CH_2(OH)_2 \\ CH_2(OH)_2 + H^+ \rightarrow CH_2\begin{smallmatrix}OH\\ OH_2^+\end{smallmatrix} \rightarrow (CH_2OH)^+ + H_2O \\ (CH_2OH)^+ + ArH \rightarrow ArCH_2OH \\ ArCH_2OH + H^+ \rightarrow ArCH_2OH_2^+ \rightarrow ArCH_2^+ + H_2O \\ ArCH_2^+ + ArH \rightarrow Ar\cdot CH_2\cdot Ar \end{cases}$$



In the last case further condensation of the same type with more phenolate ion gives diphenylmethane derivatives, a reaction of importance in the formation of bakelite.†

The other method of forming carbonium ions, the addition of H^+ to olefines, is seen in the alkylations of aromatic hydrocarbons by olefines in presence of H_2SO_4, HF, BF_3, etc. (the intermediate ions may be π-complexes, but this would not materially affect the situation). The addition of H^+ to an olefine is of course an intermediate step in the addition of hydrogen halides. The products of condensation with aromatic compounds obey Markownikoff's rule, the aromatic ring attaching itself to the more substituted end of the olefinic C=C bond. These reactions again require no special discussion.

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† See Meyer, *High Polymers*, vol. 4, 'High Polymeric Substances', Interscience Publishers, New York, 1942.

$$\left\{\begin{array}{l} \mathrm{C{=}C} + \mathrm{H}^+ \rightarrow \overset{+}{\mathrm{C}}\mathrm{{-}CH} \\ \mathrm{ArH} + \overset{+}{\mathrm{C}}\mathrm{{-}CH} \rightarrow \mathrm{Ar{-}C{-}CH} \end{array}\right.$$

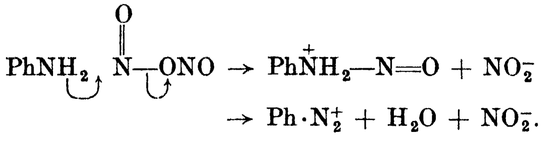
$$\left\{\begin{array}{l} \mathrm{C{=}C} + \mathrm{BF_3} \rightarrow \overset{+}{\mathrm{C}}\mathrm{{-}C{-}BF_3^-} \\ \mathrm{ArH} + \overset{+}{\mathrm{C}}\mathrm{{-}C{-}BF_3^-} \rightarrow \mathrm{Ar{-}C{-}C{-}BF_3^-} + \mathrm{H}^+ \\ \qquad\qquad\qquad\qquad \rightarrow \mathrm{Ar{-}C{-}CH} + \mathrm{BF_3}. \end{array}\right.$$

Diazonium salts

Schmidt and Muhr† have investigated the rate at which diazonium salts are formed from aniline and nitrous acid. In dilute sulphuric acid the rate is given by $k[\mathrm{PhNH_2}][\mathrm{HNO_2}]^2$ and the reaction therefore involves two molecules of free nitrous acid and one of free aniline. In dilute hydrochoric acid, however, the rate is given by

$$k_1[\mathrm{PhNH_2}][\mathrm{HNO_2}]^2 + k_2[\mathrm{PhNH_2}][\mathrm{HNO_2}][\mathrm{HCl}],$$

so here a second reaction occurs simultaneously in which one of the HNO_2 molecules is replaced by HCl. The most reasonable explanation seems to be that the active diazotizing agents are N_2O_3 or NOCl, formed from $2HNO_2$ or HNO_2+HCl in a preliminary stage. The subsequent reaction with aniline resembles an ester hydrolysis:



$$\mathrm{PhNH_2} \;\; \overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{N}}\mathrm{{-}ONO} \rightarrow \mathrm{Ph\overset{+}{N}H_2{-}N{=}O} + \mathrm{NO_2^-}$$
$$\rightarrow \mathrm{Ph{\cdot}N_2^+} + \mathrm{H_2O} + \mathrm{NO_2^-}.$$

It is interesting that other mixed anhydrides of nitrous acid are also powerful diazotizing agents.

The reaction of glycine with nitrous acid follows the same kinetics and presumably a diazonium salt is formed in that case also; but the diazonium cation is unstable and rapidly loses nitrogen to form $\mathrm{CH_2^+{\cdot}COOH}$, which then reacts with the solvent (water), giving glycollic acid.

The conversion of aliphatic amines to alcohols probably follows a similar course. In the case of aniline, however, where the diazonium salt is mesomeric and so stabilized, the ion may be written

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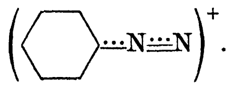
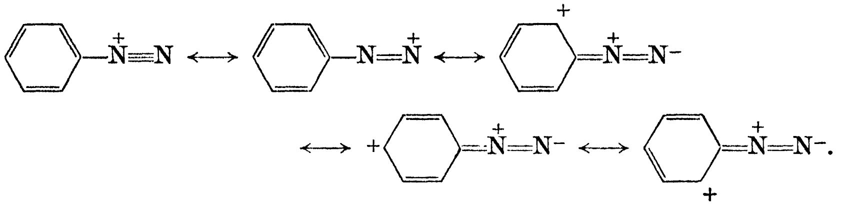
† *Ber.* 1937, B **70**, 421.

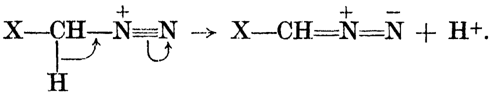


The possibilities of mesomerism are perhaps better seen in this case from resonance notation; the ion may be written as a hybrid of five structures:



The diazonium group is thus seen to have +E activity. This is shown in the *p*-halobenzenediazonium salts by the ready anionoid replacement of the *para* halogen.

A further mode of decomposition of diazonium salts is possible in the aliphatic series. Methylamine derivatives containing a strongly +E substituent give aliphatic diazo-compounds with nitrous acid. Their formation may be represented:



$$\mathrm{X{-}\underset{\displaystyle H}{CH}{-}\overset{+}{N}{\equiv}N \rightarrow X{-}CH{=}\overset{+}{N}{=}\overset{-}{N} + H^+}.$$

The reaction is facilitated by the +E substituent because the latter increases the acidity of the α-hydrogen, that is, increases its tendency to ionize. It is interesting that a powerful +I substituent can have the same effect; β:β:β-trifluoroethylamine, $CF_3{\cdot}CH_2NH_2$, gives a stable diazo-compound $CF_3{\cdot}CHN_2$ with nitrous acid.†

Rate of diazotization

Since the diazotization reaction involves anionoid attack by the amine on the nitrous acid derivative, it should be facilitated by substituents which increase the anionoid reactivity (i.e. the basicity) of the amine, hindered by substituents which decrease it. It is of course well known that amines of low basicity are much more difficult to diazotize than basic ones, and special methods are often necessary to effect reaction. In many cases it is necessary to use solutions of nitrous acid in H_2SO_4 or other strong acids; such solutions are now known to contain the NO^+ cation which is naturally the most cationoid form in which the NO group can occur.

Diazo-coupling

This reaction seems to involve a direct cationoid replacement of hydrogen by the diazonium cation; since the latter is a weakly cationoid reagent, specific activation of the nucleus by a strongly anionoid substituent is necessary. Phenols couple in alkaline solution since they are then converted to the more anionoid phenoxide ions, while aniline couples as free base, the salts being unreactive. These conclusions are confirmed by kinetic studies.[†]

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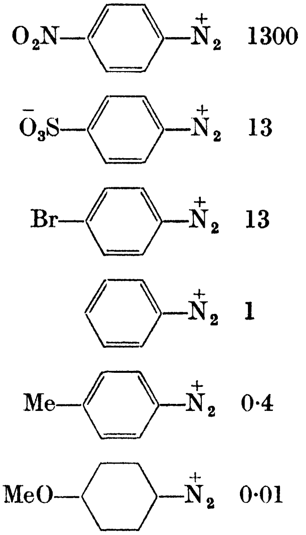
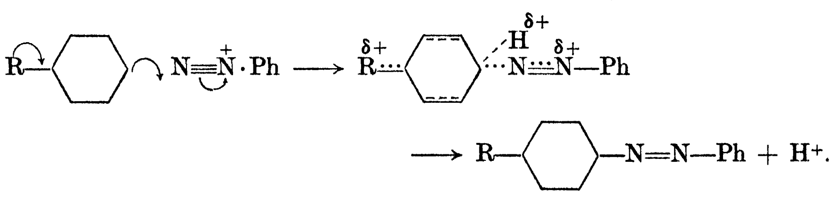
† Gilman and Jones, *J.A.C.S.* **1943, 65, 1458.**

The cationoid reactivity of the diazonium ion will be increased by positive, decreased by negative substitution. This is illustrated by the relative rates of coupling of *p*-substituted diazonium ions under standard conditions.[‡]



Moreover, diazonium salts carrying several +E substituents, e.g. picryldiazonium salts, can couple with weakly anionoid benzene derivatives such as mesitylene. The detailed mechanism of coupling may be represented:



Sandmeyer reaction

Waters[§] has suggested that cuprous salts act as catalysts in the Sandmeyer reaction by their ability to give up reversibly one electron to the diazonium salt, forming nitrogen and a phenyl radical, e.g.

$$Cu^{+} + Ph{-}N_2^{+} \rightarrow Cu^{++} + Ph\cdot + N_2$$

$$Ph\cdot + CuCl_2 \rightarrow PhCl + CuCl.$$

[†] Wistar and Bartlett, ibid. 1941, **63**, 413; Hauser and Breslow, ibid., p. 418.

[‡] Conant and Peterson, ibid. 1930, **52**, 1220.

[§] Waters, *J.C.S.* 1942, 266.

The specific catalytic activity of copper would then be due to its occurrence in two states of oxidation of comparable stability. However, Hodgson[†] has shown that cupric chloride and other metal chlorides can also act as catalysts under certain conditions, so it is very doubtful whether Waters's idea is correct. It is more likely that the mechanism is of ionic type, and that the catalytic action depends on a stabilization of the transition state for replacement by complex formation. No definite theoretical discussion is possible at present, but it seems quite likely that easily deformable anions may form the more stable transition states. Complex halide anions must be more deformable than simple halogen anions; and iodides react directly with diazonium salts, the I^- ion being much more easily deformed than are the other halogen anions (cf. p. 68).

Molecular complexes[‡]

The nature of molecular complexes was not understood until the advent of quantum theory. All attempts to formulate them in terms of primary valencies had proved unsatisfactory, and the only types of intermolecular force then known were too small to account for the stability of complexes. These forces were of two types: electrostatic attraction between polar molecules, electric dipoles being able to attract each other, and a similar electrostatic attraction due to the presence not of permanent dipoles, but of temporary ones induced by each of the molecules concerned in the other.

London showed that a third type of force between molecules was possible. Although the function ψ for a molecule apparently describes a static distribution of charge, in reality it represents the smoothed-out average of electron distribution over a long period of time. If two molecules approach each other, their mutal electrostatic attraction or repulsion will vary from moment to moment with the instantaneous configurations of the electrons in them ; but calculation shows that the electronic motions in the molecules will tend to synchronize with each other in such a way as to produce a net attraction. London showed that these 'dispersion forces' would account for almost the whole of the van der Waals forces between all but the most polar molecules. The dispersion forces vary with the polarizability of the molecules and can be calculated approximately from the polarizabilities determined empirically. Briegleb[‡] has pointed out that the heats of dissociation of a large number of molecular complexes are in semi-quantitative agreement with those calculated. These heats of dissociation are small (1–8 Cals.), very much smaller than the energies required to break primary valencies.

Recently Weiss[§] has proposed an alternative structure for these complexes. He suggests that transfer of one electron takes place from the hydrocarbon to the nitro-compound to form two odd-electron ions; e.g. with naphthalene and picric acid,

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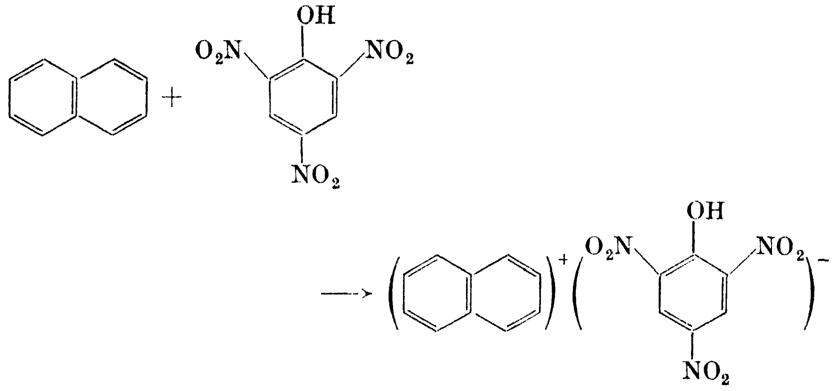
[†] Hodgson, *Chem. Rev.* 1947, **40**, 251.

[‡] For a detailed discussion see Briegleb, *Zwischenmolekulare Kräfte und Molekülstruktur*, Stuttgart, 1937.

[§] *J.C.S.* 1942, 245.



The ions are then held together by electrostatic forces. This theory seems to be quite erroneous. Firstly, there is no evidence that single electron transfers ever take place in organic chemistry unless one of the reactants is a radical or contains a metal capable of changing its valency state by one unit. A number of mechanisms for various chemical reactions have appeared in recent years which postulate such transfers, but they appear to lack any real experimental justification. Secondly, the heats of formation of molecular complexes are too low for a saline structure to be possible. Thirdly, the crystal structure and physical properties of the triiodoaniline-picric acid complex show that it is certainly not a salt.† Fourthly, Hammick and his collaborators‡ have shown that picric acid forms complexes not only with polymethylbenzenes but also with nitrobenzene, and that the stability of the complexes is greater than that of benzene regardless of the polarity of the substituent. This result would be inexplicable if Weiss's theory were correct, but follows at once if the complex-formation is due to dispersion forces. The latter depend only on the *polarizability* of the reactants and both alkylbenzenes and nitrobenzene are more polarizable than benzene. Moreover, it is interesting that dispersion forces are smaller in solvents of high dielectric constant. The Briegleb theory therefore explains why complexes are more stable in non-polar solvents, while if they had an ionic structure their stability would increase with solvent dielectric constant.

Heterocyclic compounds

(*a*) *Pyridine*

Pyridine resembles benzene in that it contains a conjugated system of six π-electrons, one being contributed by each atom in the ring. However,

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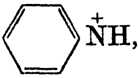
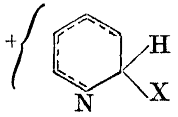
† Huse and Powell, ibid. 1943, 435.

‡ Private communication.

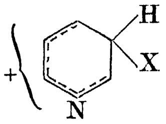
the electron affinity of nitrogen is greater than that of carbon; the π-electrons therefore tend to cluster round the nitrogen which thereby acquires a negative charge. The electronic structure of pyridine is therefore less symmetrical, and so its resonance energy smaller, than that of benzene (p. 36). Although the nitrogen atom in pyridine carries a negative charge, pyridine is less basic than ammonia. In the pyridinium ion, 

, the positive charge on the nitrogen increases its electron affinity and so reduces the electronic symmetry and resonance energy still further. This decrease in resonance energy reduces the stability of the salts and hence the basicity of pyridine.

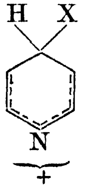
The three quinonoid formulae for the transition states for cationoid substitution in pyridine are:



(α)



(β)

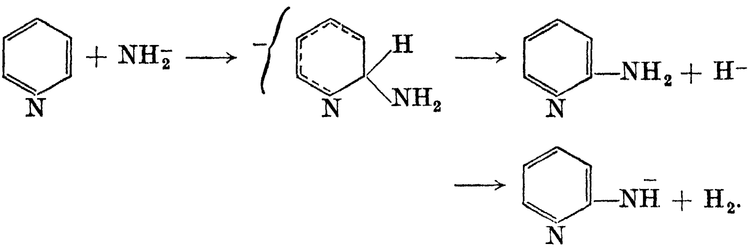


(γ)

In all three the nitrogen is included in a positively charged mesomeric system. Formation of the transition state therefore involves a removal of electrons from the nitrogen, and much more energy is required to do this than to form the corresponding transition state from benzene since the electron affinity of nitrogen is much greater than that of carbon. Therefore pyridine undergoes cationoid substitution much less readily than does benzene. Moreover, in a charged linear mesomeric system of five atoms, the charge resides mainly on the 1-, 3-, and 5-atoms. Therefore the α- and γ-transition states will be less stable than the β since in the former the nitrogen atom occupies a more highly charged position in the mesomeric cation. The situation is exactly analogous to that in nitrobenzene; the parallel is seen more clearly if we remember that a positive substituent increases the electron affinity of the atom to which it is attached, so that the group ($\rangle C—NO_2$) in nitrobenzene resembles electronically the nitrogen atom in pyridine.

Therefore pyridine is substituted with difficulty by cationoid reagents, and almost exclusively in the β-position. This effect is magnified by the acid conditions under which such reactions (nitration, sulphonation, etc.) commonly take place, since acid converts pyridine to a salt in which the electron affinity of nitrogen is still greater.

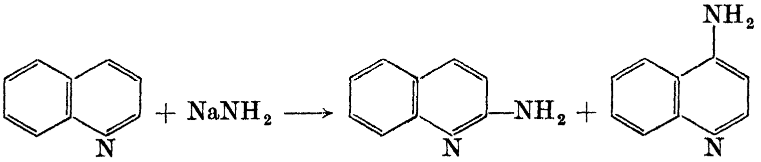
Conversely, of course, the transition states for anionoid substitution will be more stable in pyridine than benzene. Pyridine therefore undergoes anionoid substitution readily, reaction occurring mainly in the α- and γ-positions, since the nitrogen then occupies positions of largest negative charge. Direct replacement occurs with sodamide, the main product being α-aminopyridine (Chichibabin reaction).

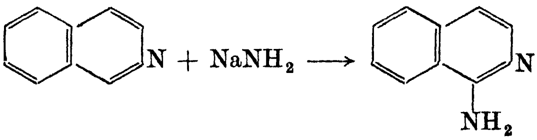


Replacement of other atoms from the α- and γ-positions also takes place readily, α- and γ-chloropyridines reacting easily with alkali to form pyridones, and with ammonia to give aminopyridines.

The side-chain reactions of pyridine also resemble those of nitrobenzene. The pyridyl group is a more strongly +E substituent than phenyl, α- and γ-pyridyl excelling the β-isomer in this respect. Thus α- and γ-picolines are stronger acids than toluene; their conjugate anions can be prepared with bases of moderate strength, and they therefore undergo aldol and Claisen type reactions with carbonyl compounds and esters. Moreover, the hydrogen atoms are exchanged for deuterium in alkaline deuterium oxide solution.† β-Picoline does not exhibit these reactions.

Just as pyridine resembles nitrobenzene in its reactions, so do quinoline and *iso*-quinoline resemble α- and β-nitronaphthalene respectively. Both undergo cationoid substitution in the benzene ring exclusively, and in the 5- and 8-positions, for the same reason that mononitronaphthalenes give 5- and 8-substitution products. Moreover, *iso*-quinoline on nitration gives mainly 5-nitro*iso*quinoline, while quinoline gives a mixture of the 5- and 8-isomers in comparable amounts. Anionoid substitution, on the other hand, takes place rather easily in the nitrogen-containing ring. Thus quinoline with sodamide gives both α- and γ-aminoquinolines, while *iso*-quinoline gives 1-amino*iso*quinoline.‡





The 3-position in *iso*-quinoline is not activated to anionoid substitution, for the same reason that the 3-position in β-naphthol is not activated to cationoid substitution.

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† Erlenmeyer, Weber, and Weissmer, *Helv. Chim. Acta*, 1938, **21**, 863, 1017.

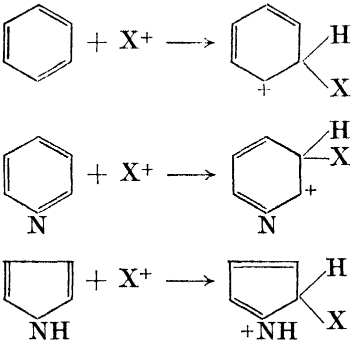
‡ For a survey of Chichibabin reactions see Leffler, *Organic Reactions*, **1**, 91.

(*b*) *Pyrrole*

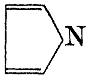
In pyrrole the nitrogen contributes two of the six π-electrons, and although it does by virtue of its superior electron affinity acquire more than its share of the common stock, it is nevertheless left with a residual positive charge. Moreover, salt-formation would give an ion in which the nitrogen had no free *p*-electrons and which would therefore not be aromatic; pyrrole is therefore an extremely weak base, since it can only form salts at the expense of its considerable resonance energy (25 Cals.). Since the salts are not aromatic, strong acids polymerize pyrrole.

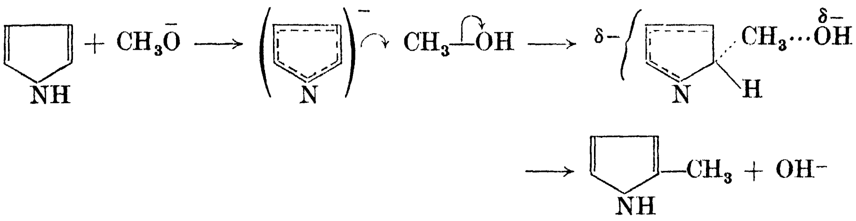
But the anion formed from pyrrole by loss of a proton from the imino-group is more symmetrical and has a higher resonance energy than pyrrole, since the negative charge reduces the electron affinity of the nitrogen to a value more comparable with that of carbon. Therefore pyrrole is a stronger acid than ammonia and readily gives metal derivatives.

Pyrrole differs completely from pyridine in that it readily undergoes cationoid substitution. The reason for this is very simple. If we write classical structures for the initial and transition states for cationoid substitution in benzene, pyridine, and pyrrole,

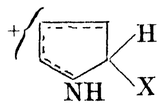


we see that in the two former compounds the rings in the transition states contain one bond less than in the initial states, while in pyrrole both states contain the same number of bonds. Since the heat of formation of a bond is at least comparable with the difference in resonance energy between the initial and transition states, or with the energy difference in pyridine due to recession of electrons from nitrogen in forming the transition state, it is evident that unusually little energy must be required to form the pyrrole transition state, and so pyrrole undergoes cationoid substitution with great ease.

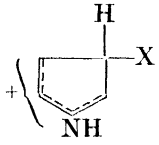
Not only will pyrrole couple with diazonium salts and react readily with halogens and other standard cationoid reagents (provided the reactions are carried out in the absence of strong acid which would resinify the pyrrole), but it will also react with quite weakly cationoid compounds such as alkyl halides (which give alkylpyrroles through an S_2 replacement of halogen by pyrryl). The pyrrole anion N^- is of course even more reactive than pyrrole since in it the lowered electron affinity of nitrogen facilitates formation of the transition state. Pyrrole is readily alkylated by heating with sodium alkoxides in alcohols, probably by an S_2 replacement of hydroxyl (cf. p. 67).



The preferential α-substitution shown by pyrrole is rather hard to explain in qualitative terms, though it can easily be shown by quantum-mechanical calculation that of the two transition states, (α) is the more stable;



(α)



(β)

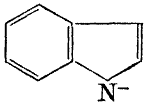
The most valid qualitative interpretation seems to be this. In a mesomeric system where one atom has an abnormally high electron affinity, the electronic symmetry is less than in a similar system where all the atoms are alike. The odd atom acquires an excess electronic charge, and so approximates more to a form in which its own p-orbital is filled at the expense of the rest of the π-bonded system. The bonds attaching the odd atom to the rest of the system are therefore of abnormally small order and have correspondingly low heats of formation. The whole effect leads to a decrease in stability of the conjugated system. Now if the odd atom is at the end of the conjugated system, only one bond will be weakened; but if it is in the middle, two will be. Therefore of two conjugated isomers, differing only in that in one the odd atom occupies one end of the conjugated system, and in the other a central position, the former will be the more stable. Therefore of the two pyrrole transition states (α) is the more stable, and so pyrrole substitutes α more readily than β.

The same argument should apply also to pyridine, implying that α-substitution should occur more readily than γ; but in practice the deactivation of both positions is so complete that no α- or γ-products can be isolated from its cationoid substitution. However, the same effect should also be observed in benzene derivatives when the electron affinity of one carbon is increased by positive substitution; and it is in fact observed in such cases that *ortho* by-products are formed to a much greater extent than *para*. Thus nitration of nitrobenzene gives appreciable amounts of *o*-dinitrobenzene but virtually no *p*-dinitrobenzene; and a similar reaction leads to the formation of undesirable by-products in the manufacture of trinitrotoluene.

The chemistry of furane and thiophene resembles that of pyrrole closely and need not be discussed in any detail. Both undergo cationoid substitution readily, and mainly in the α-position. Indeed, the ready reaction of thiophene with cationoid reagents provides the simplest method for removing it from benzene.

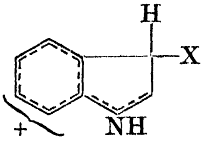
(*c*) *Indole*

Indole stands in the same relation to pyrrole that quinoline does to pyridine. The nitrogen again provides more than its share of the π-electrons; and again salt-formation with acids leads to great decrease in resonance energy; while conversion to the indolyl anion,

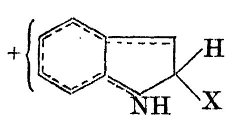


takes place with an increase in resonance energy. Indole is therefore an extremely weak base, but forms metal derivatives quite easily. No true salts of indole with acids have been isolated, and the cation, where the 5-membered ring is no longer aromatic, readily polymerizes. The picrate, styphnate, and other analogous 'salts' of indole are undoubtedly molecular complexes in which the components are held together by dispersion forces.

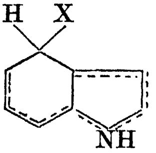
Indole undergoes cationoid substitution almost as readily as pyrrole and for the same reason; the classical structures for the initial and transition states contain the same number of annular bonds. However, in indole substitution occurs by preference in the β-position; the reason for this is obvious from an examination of the transition states, the β-state alone containing an intact benzene ring.



(β)



(α)



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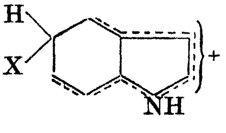

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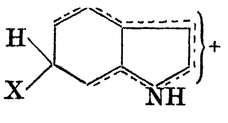

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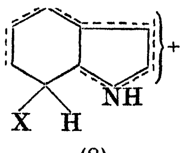
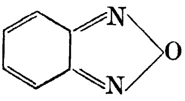


(8)

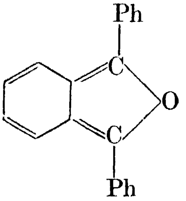
All the other transition states contain linear mesomeric systems. Since in the one for α-substitution alone the nitrogen is at one end of the mesomeric chain, it is evident that the α-position should be next to the β in reactivity. This is found to be the case.

Indolizine and iso-*indole*

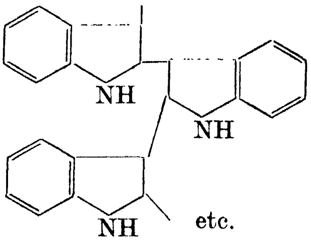
The general electronic structure of indolizine and *iso*-indole should resemble that of indole, the nitrogen atom in each case contributing two of the ten π-electrons. Indolizine is certainly an aromatic compound (p. 161), but no derivative of *iso*-indole has yet been prepared. However, *iso*-benzfurazane (VI) is known and appears from its stability to heat and acid to be aromatic; and 1:3-diphenyl*iso*benzfurane (VII) is also known and seems to be rather stable. Both these compounds are electronic analogues of *iso*-indole, and it seems likely that the failure to isolate the latter may be due to ready polymerization rather than to inherent instability. Both indole and *iso*-indole should polymerize exothermally to (VIII) and (IX), and their apparent stability as monomers will depend on the activation energies of polymerization.



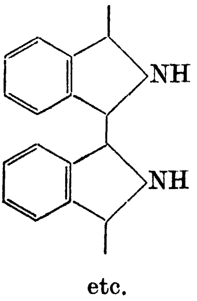
(VI)



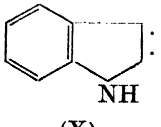
(VII)



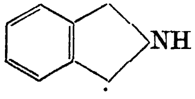
(VIII)



(IX)



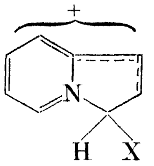
(X)



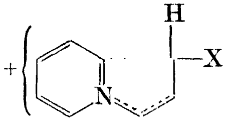
(XI)

The activation energy will be roughly proportional to the energy required to convert the monomer into a diradical form (cf. Chapter XIV) and so if the resonance energies of indole and *iso*-indole are roughly the same, as theory suggests, their ease of polymerization will depend on the resonance energies of the corresponding diradicals. Now in the indole diradical (X) one radical centre is conjugated with the benzene ring but the other is unstabilized; while in the *iso*-indole diradical (XI) both centres are conjugated with the ring. The latter should therefore be the more stable, and so *iso*-indole should polymerize more readily than indole. (The calculated resonance energies of the two radicals are 52 Cals. and 61 Cals.)

Indolizine resembles indole closely in its reactions; it is almost non-basic, but forms a molecular complex with picric acid, and it is very easily substituted by cationoid reagents, even undergoing nuclear methylation with methyl iodide (like pyrrole and indole). The orientation of the products has not been established, but they are almost certainly 1-derivatives. The transition states for 1- and 3-substitution alone contain an intact pyridinium ring:



(1)

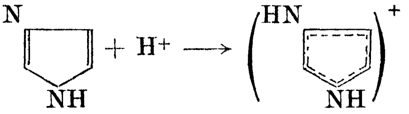


(3)

In the latter the nitrogen is at the junction of three segments of the conjugated system, while in the former it is at the junction of two only. Therefore three π-bonds are weakened in the (3) transition state by the high electron affinity of nitrogen but only two bonds in the (1) transition state. Therefore the latter should be the more stable. Coulson and Longuet-Higgins[†] have concluded from quantum-mechanical calculation that 1-substitution should be favoured, and the prediction has recently been confirmed.[‡]

Pyrazole, Iminazole, etc.

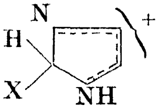
These 5-membered aromatic rings resemble pyrrole in their general electronic structure, but differ considerably from it in their reactions. With acids, for example, they form stable salts, the proton attaching itself to the second hetero atom to give cations whose symmetry, and hence their resonance energy, is greater than that of the parent base.



(The cation unlike the base, has a plane of symmetry bisecting the line joining the nitrogen atoms.) The bases themselves are, however, more symmetrical than pyrrole, since they contain two hetero atoms, and although the evidence is meagre they do seem to have rather larger resonance energies. Moreover, they react less readily than pyrrole with cationoid reagents, and their salts react less readily still, since in the transition states for substitution two hetero atoms acquire positive charges. However, iminazole will brominate, and couple with diazonium salts, under neutral or alkaline conditions, giving 2-substituted products. In the transition states for 2-substitution the nitrogen atoms are at the ends of the mesomeric cation, while in the (4) transition state one nitrogen occupies a central position.

[†] *Trans. Faraday Soc.* 1947, **43**, 87.

[‡] Burrows, Holland, and Kenyon, *J.C.S.* 1946, 1069, 1075, 1077, 1083.



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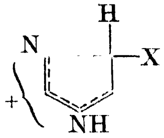
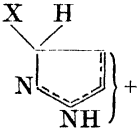


(4)

Substitution in pyrazole takes place less readily than in iminazole since in both transition states at least one nitrogen occupies a central position in the mesomeric chain. Substitution takes place in the 4-position, probably because the corresponding transition state is more symmetrical and so more stable. (The orientation of substitution in pyrrole and iminazole is correctly predicted by quantum-mechanical calculation.)



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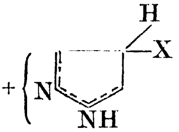
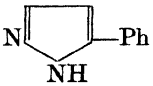


(4)

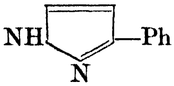
Other 5-membered rings such as oxazole, *iso*-oxazole, thiazole, etc., resemble pyrazole or iminazole so closely in their properties that no detailed consideration is necessary.

Mesohydric tautomerism

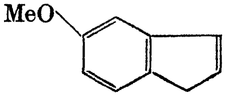
Recently Hunter† has cited a number of cases where isomers, differing only in the position of attachment of one hydrogen atom, appear to have no independent existence. Thus substituted pyrazoles and iminazoles might theoretically occur in isomeric forms; e.g.



and



but in no case have isomers been isolated. Of course the interconversion of such compounds might well occur by normal prototropy, the prototropic reactions of $\rangle$NH compounds being very rapid; but the extraordinary ease of interconversion of isomeric indenes, for example, the pair



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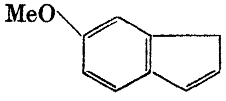

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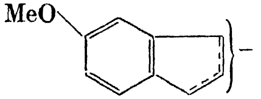
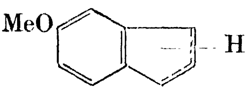
† Ibid. 1945, 806.

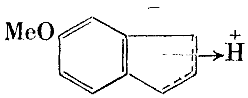
can hardly be so explained, since these indenes are extremely weak acids, and ionization to



should be slow. Hunter suggests that in all such cases the mobile hydrogen is attached by some peculiar kind of bond and is not localized definitely in the molecule. It seems very likely that this bond is actually our 'molecular bond', the compounds being π-complexes. Thus the indene could be written



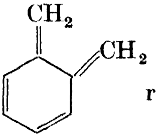
or



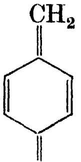
The proton will spend most of its time near the 1- and 3-carbon atoms where the negative charge in the anion would be concentrated, but it will be able to move quite easily from one atom to the other, being attached all the time to the annular π-electrons. (See also p. 223.)

Quinones

It has generally been assumed that quinones are not aromatic compounds, but this is not true. The resonance energy of *p*-benzoquinone, calculated from its heat of combustion, is about 20 Cals.; and the resonance energies of the corresponding *o*- and *p*-dimethylenecyclohexadienes calculated by quantum mechanics are still larger, i.e.



resonance energy 34 Cals.



,, ,, 29 Cals.

These values suggest that the apparent instability of quinones is more apparent than real.† Their reactivity is due to the ease with which they are converted into 'normal' aromatic compounds, whose resonance energies are still greater. Thus quinone itself by adding two electrons can pass over into the dianion of hydroquinone which has a resonance energy of

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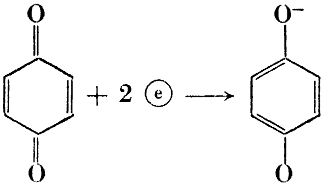
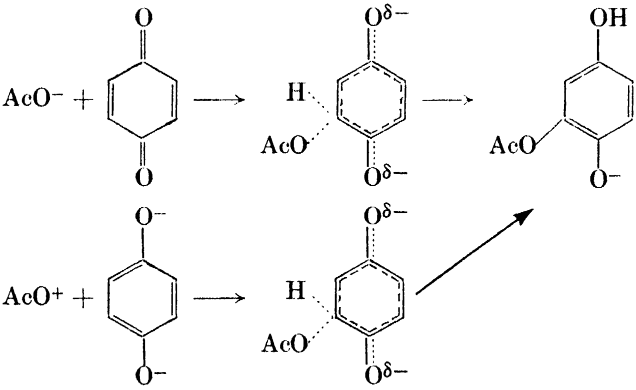
† The *para* isomer has been prepared by Szwarc and is stable in the gas phase; *J. Chem. Phys.* 1948, **16**, 128.

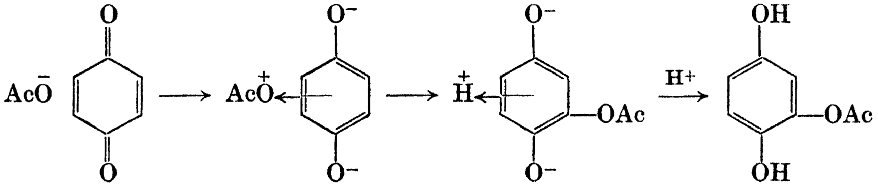
45–50 Cals. Therefore quinone has a large affinity for electrons, and so is a powerful oxidizing agent.



The 'addition reactions' of quinone can also be explained without assuming quinone to be non-aromatic. For instance, the transition state for addition of acetate ion to quinone would have the same configuration, and the same number of electrons, as the transition state for cationoid attack by an acetate cation on the dianion of hydroquinone, and the product

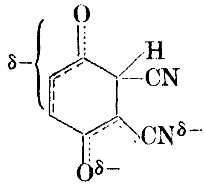


would be the same. The reactions differ only the position of two electrons in the reactants. The initial adduct is therefore presumably a π-complex, and its energy of formation from acetate anion and quinone will be smaller than from acetate cation and hydroquinone dianion, since the resonance energy of the reactants will be smaller in the former case. The reaction therefore takes place with great ease. The whole mechanism may be depicted

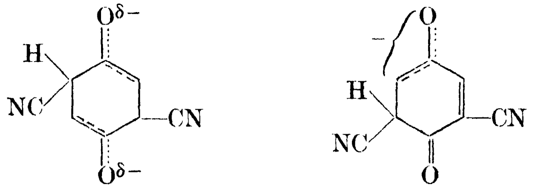


In the first step the π-complex is formed by coordination of acetate anion with an electron-deficient mesomeric system (quinone) instead of coordination of an anionoid mesomeric system (hydroquinone) with an electron-deficient acetate cation.

The orientation of 'addition' will then follow exactly the same principles as cationoid substitution of the corresponding benzene derivative, since the intermediate π-complex is the same. The rate of the reaction, being determined by the rate of formation of the π-complex from an anion and a cationoid ring, will depend on the cationoid reactivity of the latter; and positive substituents increase, and negative decrease, the cationoid reactivity of quinone. A good illustration of these points is the reaction of cyanoquinone with cyanide ion. The reaction occurs rather easily, since the +E nitrile group increases the cationoid reactivity of the nucleus. Moreover, an examination of the three possible transition states shows that in (*a*) alone the original CN group is conjugated with one of the carbonyls; therefore (*a*) is the most stable of the three and the reaction gives *o*-dicyanoquinone. The argument is identical with that given to explain the *o*-dinitration of *p*-acetanisidide (p. 166).



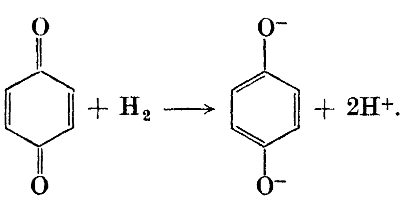
(*a*)



(*b*)

Redox potentials of quinones

Since quinone is a cationoid ring system, passing over into the anionoid hydroquinone by the uptake of two electrons, it will be stabilized more by negative substituents than will be its reduction product, while positive substituents will stabilize the reduction product more than the quinone. Therefore negatively substituted quinones are less easily reduced and are therefore weaker oxidizing agents than quinone, while positively substituted quinones are stronger oxidants. The oxidizing power of quinone is best measured by its redox potential, which is a measure of the free energy liberated in the reaction:



The redox potential should be increased by positive and decreased by negative substitution. These effects are shown very clearly in the following table of redox potentials of a number of quinone derivatives.†

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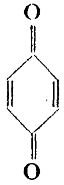
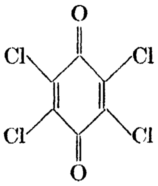
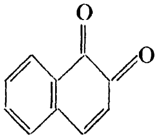
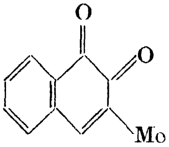
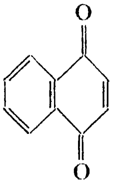
† The data are taken from Wallenfals and Möhle, *Ber.* 1943, B 76, 924.

TABLE 25

Compound	*Redox potential (MV.)*
	696
	712
	578
	543
	488
2-Methyl	422
2-Ethyl	419
2-Methoxy	369
2-Hydroxy	362
2-Hydroxy-3-methyl	306
2:3-Dihydroxy	288
6-Methyl-2:3-dihydroxy	256
6-Bromo-2:3-dihydroxy	321

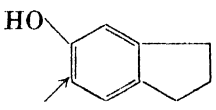
The Mills–Nixon effect

In 1930 Mills and Nixon† reported that while 5-hydroxyhydrindene (XII) couples with diazonium salts in the 6-position, 6-hydroxytetralin (XIII) couples in the 5-position. They suggested that in these compounds

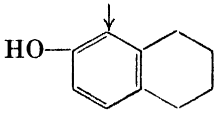
---

† *J.C.S.* 1930, 2510.

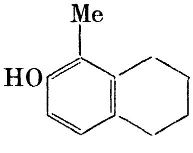
'fixation' of the double bonds occurs in the positions indicated, the diazonium salt coupling only at a carbon atom separated from hydroxyl by a double bond. No such effects were observed with 3:4-dimethylphenol.



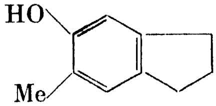
(XII)



(XIII)



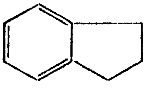
(XIV)



(XV)

The explanation given by Mills and Nixon cannot be accepted since the benzene rings in both hydrindene and tetralin are unquestionably mesomeric.† It has since been shown that their conclusions were partly incorrect, since (XIII) brominates in both the 5- and 7-positions and 5-methyl-6-hydroxytetralin (XIV) couples readily in the 7-position;‡ while 6-methyl-5-hydroxyhydrindene (XV) will react with cationoid reagents in the 4-position.‡ However, the latter reactions take place only with difficulty, so there is evidence that some abnormal effect does operate in the case of 5-hydroxyhydrindene although not to the extent that Mills and Nixon supposed.

There is no necessity to assume actual bond-fixation in order to explain the small differences in reactivity observed. A small strain-energy difference in the transition states, due to the 5-membered ring constraining the benzene ring in some way, would be sufficient. Wheland§ suggested that the 5-membered ring acts like a spring, tending to stretch the bond common to the rings and so making the Kekulé form



predominate in the hydrindene resonance hybrid. But recently Coulson and Longuet-Higgins‖ have shown theoretically that the 5-membered ring must actually tend to *compress* the common bond and so Wheland's explanation is undoubtedly incorrect. However, the 5:6 bond is correspondingly stretched by the strain due to the adjacent 5-membered ring; Coulson and Longuet-Higgins therefore suggest that the Mills–Nixon effect is due to strain differences in the transition states for substitution in the 4- and 6-

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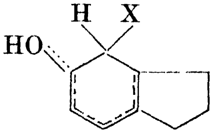
† Sidgwick and Springall, *J.C.S.* 1936, 1532; Kossiakoff and Springall, *J.A.C.S.* 1941, **63**, 2223; Kistiakowsky, *vide* p. 35.

‡ Fieser and Lothrop, *J.A.C.S.* 1936, **58**, 2050.

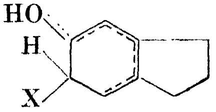
§ *J.A.C.S.* 1942, **64**, 900.

‖ *Trans. Faraday Soc.* 1946, **42**, 756.

positions; in the transition state (*a*) for 4-substitution in 5-hydroxyhydrindene, the 4:5 bond will be almost single but the 5:6 bond will have a higher order (since it forms part of a conjugated system).



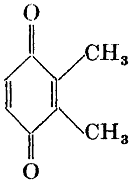
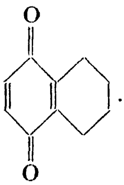
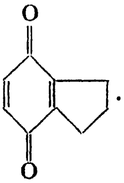
(*a*)



(*b*)

In the transition state (*b*) for 6-substitution, the 5:6 bond is virtually single. Therefore in (*b*) the 5:6 bond is of lower order and therefore longer than in (*a*), and so the strain-effect tending to stretch the 5:6 bond favours the formation of (*b*) rather than (*a*) and consequently facilitates substitution in the 6-position.

That the strain-effect is real has recently been shown by Arnold and Zaugg.† The 2:3 and 5:6 bonds in *p*-hydrindenequinone are shorter than the corresponding bonds in 4:7-dihydroxyhydrindene. Any strain-effect should consequently alter the relative stabilities of the two compounds, and hence the redox potential of the quinone. Arnold and Zaugg supposed that the main effect of the 5-membered ring would be to stretch the bond common to the rings, when *p*-hydrindenequinone should be a stronger oxidant than 2:3-dimethylbenzoquinone. This conclusion is correct, as the following data show, but the work of Coulson and Longuet-Higgins makes it possible that the dominant cause is a stretching of the 5:6 bond and not of the 2:3 bond.

Compound	*Redox potential* (*M V.*)
	588
	585
	641

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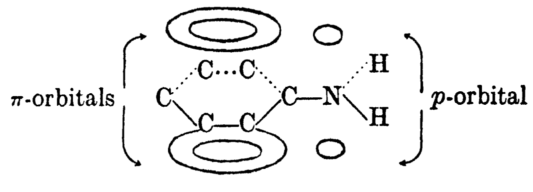
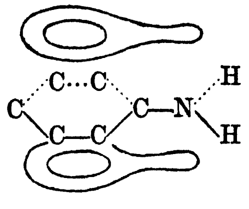
† *J.A.C.S.* **1941, 63, 1317.**

Steric inhibition of mesomerism

For *p*- or π-orbitals to coalesce into extended π-orbitals it is necessary that they should overlap; this can happen only if the molecule has an appropriate stereochemical configuration. For instance, the odd *p*-orbitals of the methylene groups in the diradical $—CH_2—CH_2—$ can overlap only if they are parallel, and the whole molecule is consequently coplanar. If one methylene group is twisted through 90°, overlapping becomes small and the π-bond practically vanishes. A similar restriction must apply to conjugation of a $\pm$E substituent with a benzene ring. In aniline, for instance, the nitrogen *p*-orbital (XVI) can overlap efficiently with the annular π-orbitals only if the $—NH_2$ group is coplanar with the ring (XVII). If the amino group is forced out of coplanarity with the ring, the mesomerism will be reduced.



(XVI)



(XVII)

In an *o*-substituted aniline derivative, the amino group may be forced out of coplanarity with the ring and the conjugation of nitrogen with the ring thus inhibited. This effect should be noticeable in any connexion where the conjugation is of importance. In a hindered aniline the amino group should be more strongly basic and affect the reactivity of the ring less than in an unhindered aniline; and the dipole moment and light absorption should not show the usual effects of conjugation. All these phenomena have been observed in *o*-substituted dimethylaniline derivatives, but not in derivatives of aniline itself since the $—NH_2$ group is apparently too small to suffer appreciable hindrance.

Similar effects should also be observed with other bulky $\pm$E substituents, and actually have been in the case of the nitro, acyl, and phenyl groups. Here again the smaller formyl is apparently not hindered by normal *o*-substituents. Some examples of this 'steric inhibition of mesomerism' follow.

1. *Effect on dipole moment*

Conjugation of a $\pm$E substituent with the ring produces an electric moment in a molecule (p. 38), which in the case of the $—NR_2$ and $—CO \cdot R$ groups reinforces the normal moment of the group. Nitrobenzene, for example, has a larger dipole moment than nitromethane. Any steric hindrance which reduces this conjugation will then also reduce the total dipole moment. Birtles and Hampson† first established the reality of this effect. They compared the dipole moments of a number of benzene, durene, and mesitylene derivatives. Since durene and mesitylene are themselves non-polar, being symmetrical, the moments of their derivatives would be the same as those of the corresponding benzene derivatives if no abnormal factors were operating; if anything, they should be larger, since durene and mesitylene are more polarizable than benzene. Some results obtained by Birtles and Hampson and by later workers† are given in Table 26. The effect is negligible with the small —NH_2, —OH, —Br, and —CHO groups, confirming that mechanical hindrance is the relevant factor.

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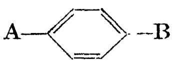
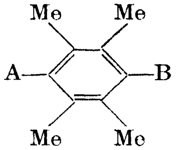
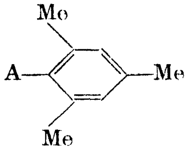
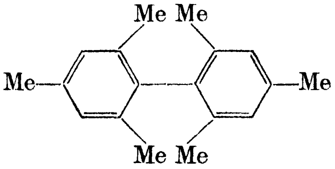
† *J.C.S.* 1937, 10.

TABLE 26

Substituents		*Dipole moment in D*		
A	B			
NO_2	H	3·95	3·39	. .
NMe_2	,,	1·58	. .	1·03
NH_2	,,	1·53	1·39	1·40
OH	,,	1·61	1·68	. .
Br	,,	1·52	1·55	. .
CH_3·CO	,,	2·88	2·68	2·71
H·CO	,,	2·92	. .	2·96
Cl·CO	,,	3·32	. .	2·95
NO_2	NMe_2	6·87	4·11	. .
,,	OH	5·04	4·08	. .
,,	Br	2·65	2·36	. .

It is particularly striking that in cases where the moments of correspondingly hindered durene and mesitylene derivatives have been determined, the two values agree very closely.



(XVIII)

2. *Effect on light absorption*

The ultra-violet absorption spectrum of diphenyl differs considerably from that of benzene, due to conjugation between the rings. In dimesityl (XVIII), however, the rings are forced out of coplanarity‡ and the conjugation between them is destroyed. Therefore the absorption spectrum of (XVIII) is almost identical with that of mesitylene but quite different to that of diphenyl.[†] A number of similar cases have been reported by Rodebush and his collaborators,[‡] who find that the alteration in the spectrum runs parallel to the ease of resolution of corresponding unsymmetrical diphenyls, both effects depending on the size of the *ortho* substituents. The inhibition of mesomerism in durene and mesitylene derivatives is also shown by their Raman spectra;[§] esters, ketones, and nitro-compounds show the effect, but the aldehydes do not (cf. the previous section).

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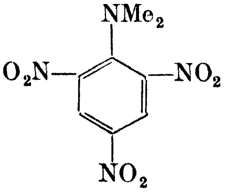
† Ingham and Hampson, ibid. 1939, 981; Kadesch and Weller, *J.A.C.S.* 1941, 63, 1310.

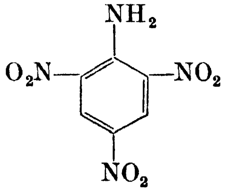
‡ This is of course shown by the optical activity of the 3:3′-diamino derivative.

3. *Effect on basic strength of anilines, etc.*

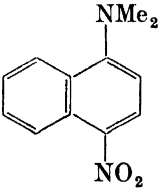
Hammett and Paul[||] observed that dimethylpicramide (XIX) is a much stronger base than picramide (XX), the corresponding basic pK's being about 18·7 and 23·3. The basicity of picramide is very small because the +E activity of the ring is greatly increased by the three nitro groups. In dimethylpicramide, the NMe_2 and two NO_2 groups hinder one another, so that the conjugation between the latter and the ring is reduced and so also the +E activity of the ring. Moreover, the conjugation between the amino group and the ring is likewise decreased. The net effect is a large increase in basicity. Wheland[††] has shown that a similar effect can be detected in dimethyl-*o*-toluidine and other related compounds. Moreover, 4-nitrodimethyl-α-naphthylamine (XIX) is a stronger base[‡‡] than 4-nitro-α-naphthylamine (XX), presumably because the more bulky NMe_2 group is pushed out of coplanarity with the ring by the adjacent *peri*-CH group.



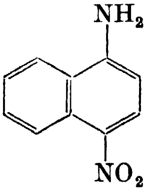
(XIX)



(XX)



(XXI)



(XXII)

The analogous effect on acid strengths has also been observed. Thus *tris*-(*p*-nitrophenyl)methane (XXIII) is quite strongly acid, its sodium salt being stable in aqueous alcohol. It is much more acidic than triphenylmethane, the +E activity of the phenyl groups being increased by the +E substituents. But *tris*-(3:5-dimethyl-4-nitrophenyl)methane (XXIV) is a much weaker acid† than (XXIII) since in it the +E action of the NO_2 groups is reduced by steric hindrance.

[†] Pickett, Walter, and Franco, *J.A.C.S.* 1936, **58**, 2296.

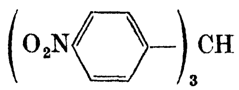
[‡] O. Shaughnessy and Rodebush, ibid. 1940, **62**, 2906; Williamson and Rodebush, ibid. 1941, **63**, 3018.

[§] Saunders, Murray, and Cleveland, ibid. p. 3121; Wittek, *Z. phys. Chem.* 1942, B **52**, 315.

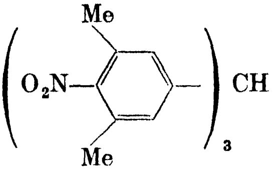
[||] *J.A.C.S.* 1934, **56**, 827.

[††] *The Theory of Resonance*, John Wiley, 1944, p. 189.

[‡‡] Arnold, Peirce, and Barnes, *J.A.C.S.* 1940, **62**, 1627.



(XXIII)



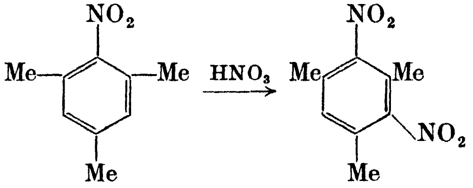
(XXIV)

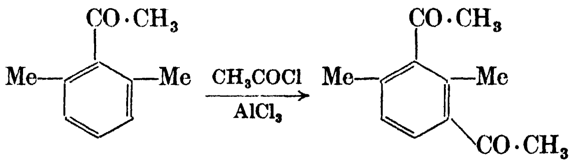
In this connexion it is interesting that X-ray crystallography shows‡ that in picryl iodide the *o*-nitro groups are perpendicular to the ring and C—N bonds have the normal single-bond length of 1·45 A, indicating that the nitro groups are not conjugated with the ring; while the *para*-NO_2 is coplanar with the ring and the C—N bond length is only 1·35 A.

4. *Effect on chemical reactivity*

A number of cases are now known where the steric inhibition of mesomerism leads to anomalies in reactivity. Perhaps the best example is the failure of *o*-substituted dimethylanilines, e.g. dimethyl-*o*-toluidine, to nitrosate in the position *para* to nitrogen. This effect has long been known and was vaguely ascribed to steric hindrance, but it was never clear how a methyl in the position *ortho* to nitrogen could affect the reactivity of the *para* position.

Here the —E activity of NMe_2 is sterically inhibited. The converse hindrance of deactivating effects is well shown by the very ready dinitration of mesitylene, and by the reaction of 2:6-dimethylacetophenone with acetyl chloride and aluminium chloride to give 2:4-diacetyl-*m*-xylene. (Normally a second acyl group cannot be introduced into acetophenone or its alkyl derivatives by the Friedel–Craft reaction, but here the +E NO_2 or Ac groups are sterically inhibited.)





The same thing happens in anionoid replacements. Kenner and his collaborators† have found that in the anionoid replacement by ammonia of one nitro group in various substituted *o*- and *p*-dinitrobenzenes, the *more* hindered nitro group is replaced; e.g.

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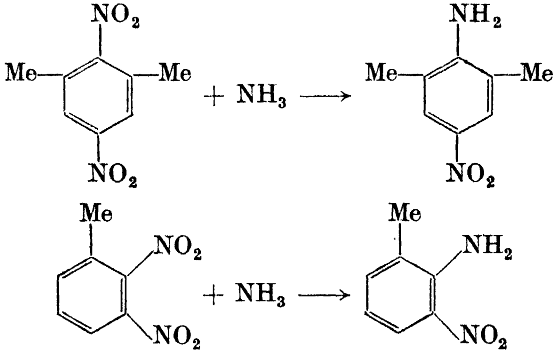
† Wheland and Danish, ibid. p. 1125.

‡ Huse and Powell, *J.C.S.* 1940, 1398.

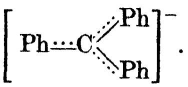


These results are particularly surprising since —I alkyl groups should reduce the rate of anionoid replacement more in the *ortho* than in the *meta* position (p. 167), and so it might be expected that in each case the *less* hindered nitro group would be replaced, on both electronic and stereochemical grounds. The explanation must be that the +E effect of the more hindered NO_2 group is reduced by hindrance, and hence its activation of anionoid replacement of the less hindered NO_2; therefore the less hindered group activates replacement of the more hindered one more strongly than the latter activates replacement of it.

One further example of hindrance in substitution reactions may be cited. The exchange of hydrogen for deuterium in an aromatic compound is a cationoid replacement, the reagent being the D^+ cation. The rate of replacement in *o*-halogenated dimethylanilines falls‡ in the series $F > Cl > Br$. Since the hydrogens replaced are those *o*–*p* to the nitrogen, or *m*- to halogen, the halogen should exert its +I effect and retard the reaction. And since the +I effect of halogen falls in the series $F > Cl > Br$, the reaction rate would on simple electronic grounds be expected to rise in the same series. The experimental results can only mean that the main function of halogen in altering the reaction rate is not electronic but steric. It prevents the nitrogen atom from conjugating with the ring. This steric effect will be greater, the larger the halogen atom, and so the effectiveness rises in the series $F < Cl < Br$.

Other examples

Triphenylmethane is appreciably acidic because the corresponding anion is mesomeric:



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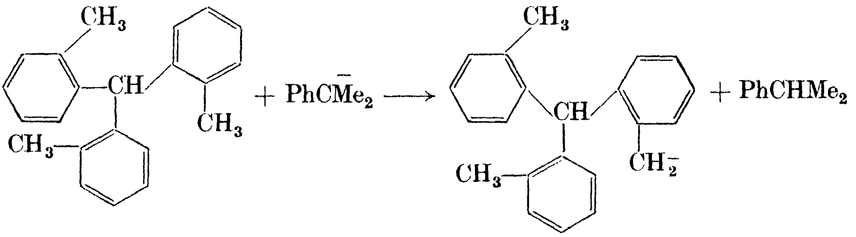
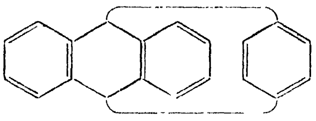
† Ibbotson and Kenner, *J.C.S.* 1923, **123**, 1260; Burton and Kenner, ibid. 1921, **119**, 1047; Kenner and Perkin, ibid. 1920, **117**, 852.

‡ Brown, Widger, and Letang, *J.A.C.S.* 1939, **61**, 2597.

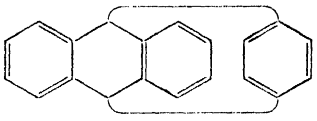
For this mesomerism to be possible the ion must have a planar configuration. Actually mutual mechanical obstruction forces the phenyl groups out of the plane to some extent, but not sufficiently to destroy their conjugation with the central carbon. However, in *tris*-(*o*-tolyl)methane the *o*-methyls obstruct the planar configuration so much that the stability of the triphenylmethyl anion is greatly reduced and so also the acidity of the central methine group. Indeed, the central hydrogen becomes less acidic than the lateral methyl hydrogens, and so treatment with phenyl*iso*propyl potassium metallates the latter.† Toluene is of course a much weaker acid than triphenylmethane.



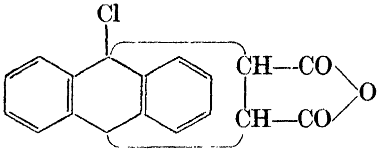
Triptycene (XXV) fails to react at all with phenyl*iso*propyl potassium,† again because the corresponding anion (XXVI) could not adopt a planar configuration.



(XXV)



(XXVI)



(XXVII)

A similar effect is seen in carbonium ions, the stability of which is greatly reduced if they are prevented from adopting a planar configuration in which attached groups can conjugate or hyperconjugate with the central carbon. Thus benzhydryl chloride normally hydrolyses rapidly by a $-\mathrm{S}_1$ mechanism; but the adduct (XXVII) of maleic anhydride with 9-chloroanthracene is unchanged by prolonged boiling with strong potash,‡ apart from hydrolysis of the anhydride. Ionization of the chlorine is repressed because the resulting carbonium ion would not be planar, while a $-\mathrm{S}_2$ replacement is impossible because the hydroxyl cannot approach the carbon from the side opposite the chlorine (cf. p. 63), and because Walden inversion cannot occur.

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† Bartlett and Jones, ibid. 1942, **64**, 1837.

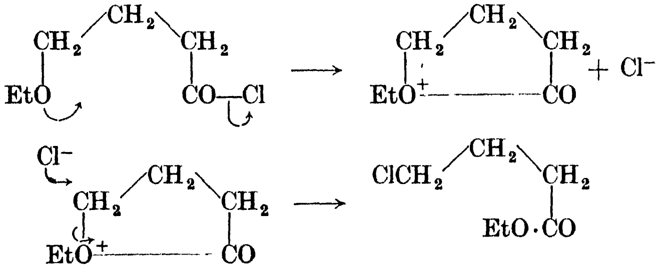
‡ Bartlett et al., ibid. 1939, **61**, 3184; 1940, **62**, 1183; 1942, **64**, 2649.

Other examples of steric inhibition of mesomerism will be found throughout this book, but those given here will suffice to show its importance. In discussing the mechanism of any reaction it is most necessary to remember that the stereochemistry of the electronic orbitals in the reactants, intermediates, and products plays quite as important a part as the stereochemical arrangement of the atomic nuclei.

CHAPTER X

MOLECULAR REARRANGEMENTS: ALIPHATIC SERIES

A MOLECULAR rearrangement may be defined as a reaction accompanied by the unexpected migration of an atom or group. Such reactions may be divided into three categories. Those of the first category are rearrangements only in name. Although a migration of a group seems to occur, detailed analysis shows that the overall reaction actually takes place in a series of 'normal' stages; in one of these the migrating group is completely detached from the parent molecule, and in a subsequent stage reattached at a different point. In the intermediate period both the migrating group and the truncated molecule whence it came are present as separate entities, and may react in some quite different way with other compounds present. Prototropic and anionoid tautomerism are good examples; in the former the mesomeric anion, formed by removal of the migrating proton, may react with other cationoid reagents in the system (e.g. D^+, Br_2); in the latter the mesomeric cation may combine with a foreign anion. These pseudo-rearrangements need not be considered in any detail since they are puzzling only while the details of their mechanisms are unknown. Two further illustrations are the oxazole rearrangements (p. 87), and the amusing rearrangement of γ- and δ-ethoxyalkyl carboxylic acid chlorides to the isomeric chloroesters[†] a reaction which undoubtedly proceeds by two normal anionoid replacements:



In a true rearrangement migration occurs in a single stage of the reaction, and the migrating group remains attached to the parent molecule during the whole period of migration. It is admittedly very difficult to establish these points definitely in any given case. The evidence is usually of three kinds. Firstly, it may be shown that the migrating group is never set free in the system, either as an ion or radical, by adding substances to the system which would combine at once with such an intermediate. Thus in the neopentyl rearrangements, discussed in detail below, it is certain that the reaction does not involve fission and resynthesis, since no methanol

$$Me_3C{-}CH_2^+ \rightarrow Me_2C{=}CH_2 + Me^+$$

$$Me_2C{=}CH_2 + Me^+ \rightarrow Me_2\overset{+}{C}{-}CH_2Me$$

[†] Prelog, Heimbach, and Juhász, *Ber.* 1941, **74** B, 1702.

or *iso*-butene is formed when the rearrangements are carried out in water. Secondly, it may be found that if the migrating group is optically active, the asymmetric centre being the point of attachment to the rest of the molecule, the rearrangement product is also optically active; in that case the migrating group can never be set free as an ion or radical since such an ion or radical would at once racemize. A good illustration is the rearrangement of optically active tropic azide to active *d*-phenylethyl *iso*-cyanate (p. 221). And thirdly, it may be shown that fission and resynthesis, if it took place, would give a different product to that actually obtained. Thus *o*- and *p*-toluenesulphonic acids are mutually interconverted by sulphuric acid, but the reaction does not take place by fission to toluene and sulphonic acid followed by resulphonation; because *m*-toluenesulphonic acid is formed in the sulphonation of toluene and is not rearranged by sulphuric acid, while in the *o*–*p* interconversion no *meta* isomer is formed.

True rearrangements can be divided into two main categories. The first, which will be discussed in the present chapter, comprises reactions in the aliphatic series where a true migration of an atom or group takes place from one atom to an adjacent atom in the molecule. The other category comprises aromatic rearrangements where the migration takes place from one position to another in an aromatic ring, and will be discussed in the following chapter.

Carbonium ion rearrangements

A large group of aliphatic rearrangements apparently involves the formation and rearrangement of intermediate carbonium ions. Three stages can in principle be distinguished, the formation, rearrangement, and further reaction of the ion, but in practice it is never possible to establish definitely whether the stages are all separate or if two of them occur simultaneously in single adiabatic processes. The main evidence that the reactions are true rearrangements is the non-formation of by-products from any possible intermediates of any mechanism involving fission and resynthesis. It will be convenient to set out the main examples with the evidence that carbonium ions are intermediates, and then to discuss their electronic mechanism in general terms.

Simple carbonium ion rearrangements

Whitmore and his collaborators have established that all reactions where a neopentyl cation would be expected as an intermediate give derivatives of *tert*-amyl alcohol. Thus neopentyl alcohol gives *tert*-amyl bromide with hydrogen bromide,† while neopentyl iodide gives *tert*-amyl acetate with silver acetate.‡ Since the acid-catalysed dehydration of alcohols almost certainly involves —S_1 mechanism (p. 114), and since the silver-catalysed solvolysis of halides also involves carbonium ion intermediates (p. 81), it seems fairly certain that the first step in these reactions is the formation of neopentyl cations.

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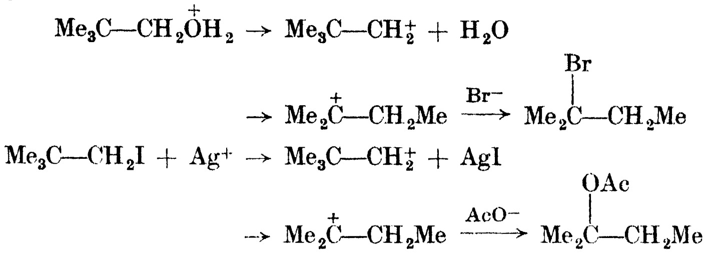
† Whitmore and Rothrock, *J.A.C.S.* 1932, **54**, 3431.

‡ Whitmore, Wittle, and Popkin, ibid. 1939, **61**, 1586.



$$\mathrm{Me_3C{-}CH_2\overset{+}{O}H_2} \rightarrow \mathrm{Me_3C{-}CH_2^+} + \mathrm{H_2O}$$

$$\rightarrow \mathrm{Me_2\overset{+}{C}{-}CH_2Me} \xrightarrow{\mathrm{Br^-}} \mathrm{Me_2\overset{\overset{Br}{|}}{C}{-}CH_2Me}$$

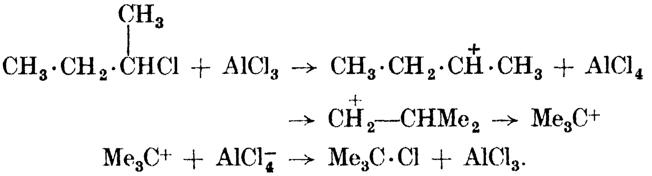
$$\mathrm{Me_3C{-}CH_2I} + \mathrm{Ag^+} \rightarrow \mathrm{Me_3C{-}CH_2^+} + \mathrm{AgI}$$

$$\rightarrow \mathrm{Me_2\overset{+}{C}{-}CH_2Me} \xrightarrow{\mathrm{AcO^-}} \mathrm{Me_2\overset{\overset{OAc}{|}}{C}{-}CH_2Me}$$

This conclusion has recently been confirmed by Dostrovsky and Hughes (p. 76), who have shown that the $-S_1$ solvolysis of neopentyl halides gives *tert*-amyl derivatives, while the $-S_2$ replacement of halogen by ethoxyl ion gives neopentyl ethyl ether.[†]

It seems impossible to explain these reactions in any terms other than a direct rearrangement of the neopentyl cation.

This rearrangement of alkyl cations seems to be very general although there is very little direct evidence in other cases for the mechanism. Thus alkyl halides are frequently isomerized by aluminium chloride, a reagent known to convert alkyl halides to alkyl cations: e.g.



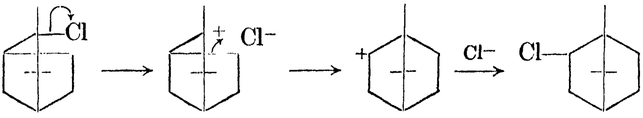
$$\mathrm{CH_3{\cdot}CH_2{\cdot}\overset{\overset{CH_3}{|}}{C}HCl} + \mathrm{AlCl_3} \rightarrow \mathrm{CH_3{\cdot}CH_2{\cdot}\overset{+}{C}H{\cdot}CH_3} + \mathrm{AlCl_4}$$

$$\rightarrow \mathrm{\overset{+}{C}H_2{-}CHMe_2} \rightarrow \mathrm{Me_3C^+}$$

$$\mathrm{Me_3C^+} + \mathrm{AlCl_4^-} \rightarrow \mathrm{Me_3C{\cdot}Cl} + \mathrm{AlCl_3}.$$

In this case there are two migrations, one of methyl, one of hydrogen.

A similar much-investigated reaction is the rearrangement of camphene hydrochloride (I) to *iso*-bornyl chloride (III). The reaction is almost



(I) (II) (II*a*) (III)

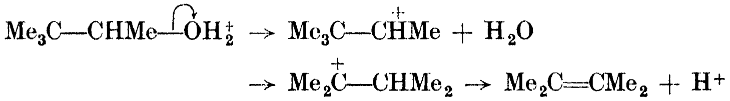
instantaneous in ionizing solvents but slow in chlorobenzene. The rate in the latter solvent is enormously increased by traces of metal halides ($SnCl_4$, $SbCl_5$) which are known to promote ionization of alkyl halides (they are effective Friedel–Craft catalysts). Moreover, the rearrangements of camphyl bromide and chlorocymenesulphonate are faster than that of the chloride while rearrangement of the trichloroacetate is slower;[‡] the order of rates follows the order of strengths of the corresponding acids. Both these effects suggest strongly that ionization to the cation (II) is the first step, and that the reaction follows the course indicated above. The rearrangement of (II) to (II*a*) involves an intramolecular alkyl migration.

[†] Whitmore, Sommer, and Gold (*J.A.C.S.* 1947, **69**, 1976) have also shown that in siliconeopentyl chloride, $Me_3Si{\cdot}CH_2Cl$, S_2 replacement of chlorine gives normal products, but S_1 replacement leads to rearrangement; thus $AlCl_3$ isomerizes the chloride to $Me_2EtSiCl$.

[‡] Bartlett and Pöckel, *J.A.C.S.* 1938, **60**, 1585.

Wagner–Meerwein rearrangement

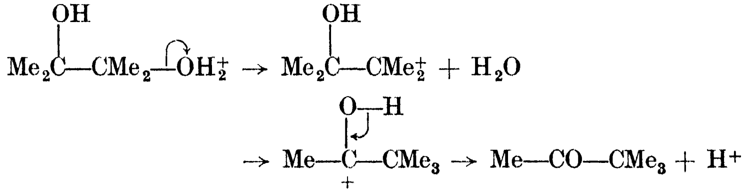
The simple carbonium ion rearrangements are analogous to $-S_1$ replacements. The Wagner–Meerwein rearrangement is the corresponding counterpart of a $-S_1$ elimination, the intermediate cation losing a proton only after rearrangement. The acid catalysed dehydration of alcohols seems to involve an intermediate cation (p. 114); and so dehydration accompanied by rearrangement, as in methyl *tert*-butyl carbinol, presumably takes place by rearrangement of an intermediate cation.



$$\mathrm{Me_3C{-}CHMe{-}OH_2^+} \rightarrow \mathrm{Me_3C{-}\overset{+}{C}HMe} + \mathrm{H_2O}$$
$$\rightarrow \mathrm{Me_2\overset{+}{C}{-}CHMe_2} \rightarrow \mathrm{Me_2C{=}CMe_2} + \mathrm{H^+}$$

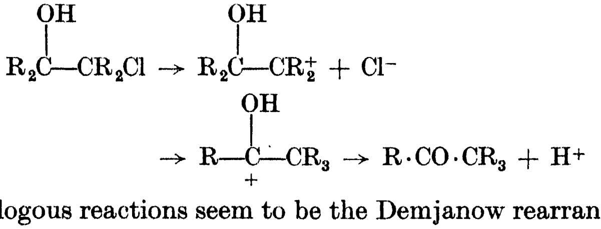
Pinacol-pinacoline rearrangement

This reaction seems to resemble formally the Wagner–Meerwein rearrangement, but the carbonium ion loses a proton to form a carbonyl compound. (The mechanism follows only from analogy.)



$$\mathrm{Me_2\overset{OH}{\overset{|}{C}}{-}CMe_2{-}OH_2^+} \rightarrow \mathrm{Me_2\overset{OH}{\overset{|}{C}}{-}CMe_2^+} + \mathrm{H_2O}$$
$$\rightarrow \mathrm{Me{-}\underset{+}{\overset{O-H}{\overset{|}{C}}}{-}CMe_3} \rightarrow \mathrm{Me{-}CO{-}CMe_3} + \mathrm{H^+}$$

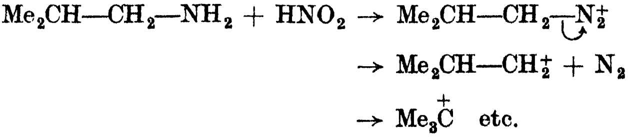
The halohydrin rearrangement follows the same pattern:



$$\mathrm{R_2\overset{OH}{\overset{|}{C}}{-}CR_2Cl} \rightarrow \mathrm{R_2\overset{OH}{\overset{|}{C}}{-}CR_2^+} + \mathrm{Cl^-}$$
$$\rightarrow \mathrm{R{-}\underset{+}{\overset{OH}{\overset{|}{C}}}{-}CR_3} \rightarrow \mathrm{R{\cdot}CO{\cdot}CR_3} + \mathrm{H^+}$$

Further analogous reactions seem to be the Demjanow rearrangement and the pinacolic deamination of β-aminoalcohols. Kinetic studies (p. 181) suggest strongly that a diazonium salt is formed as an intermediate in the reaction of aliphatic amines with nitrous acid, and analogy suggests that in the rearrangements this splits into nitrogen and a carbonium ion, e.g.†

(1)



$$\mathrm{Me_2CH{-}CH_2{-}NH_2} + \mathrm{HNO_2} \rightarrow \mathrm{Me_2CH{-}CH_2{-}N_2^+}$$
$$\rightarrow \mathrm{Me_2CH{-}CH_2^+} + \mathrm{N_2}$$
$$\rightarrow \mathrm{Me_3\overset{+}{C}} \quad \text{etc.}$$

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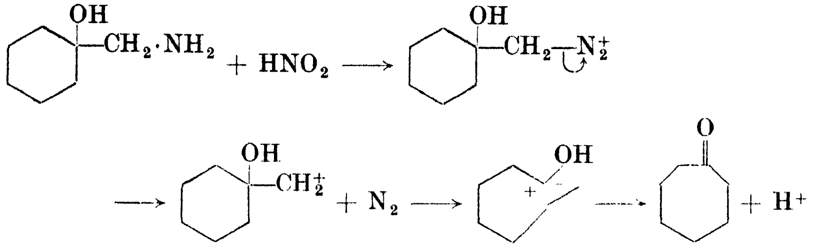
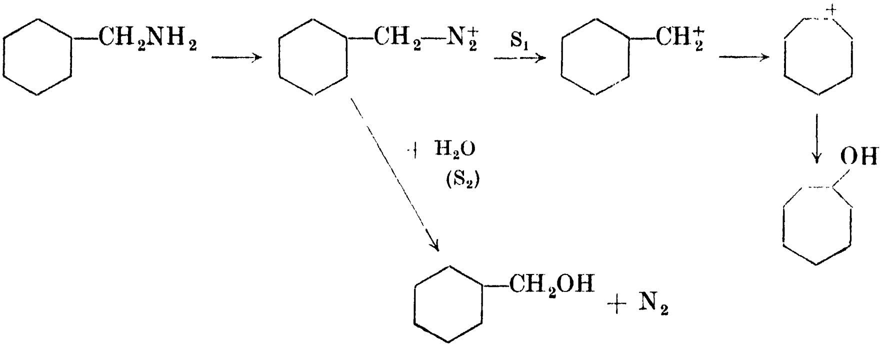
† Henry, *Compt. rend.* 1907, **145**, 899; Tchoubar, ibid. 1941, **212**, 195.

(2)

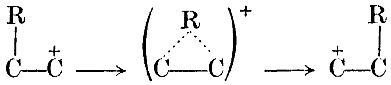


The formation of 'normal' alcohols as by-products of the Demjanow reaction may take place by a $-S_2$ replacement of $-N_2^+$, just as the $-S_2$ replacement of halogen by ethoxyl in neopentyl halides gives the 'normal' neopentyl ether.



Mechanism of the carbonium ion rearrangements

These rearrangements are all of the type



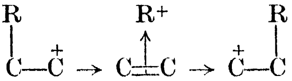
$$\overset{R}{\overset{|}{C}}-\overset{+}{C} \longrightarrow \left(\overset{R}{C\cdots C}\right)^{+} \longrightarrow \overset{+}{C}-\overset{R}{\overset{|}{C}}$$

In the transition state the migrating group R is held by bonds of some kind to two different carbon atoms. The classical electronic explanation has been that the reaction resembles a $+S_2$ replacement and that the transition state has an analogous structure. This idea is definitely inadequate. If the bonds between R and the two carbons in the transition state were analogous to those in, say, the transition state

$$\overset{-}{HO} \quad R-I \rightarrow \overset{\delta-}{HO}\cdots R\cdots\overset{\delta-}{I}$$

it would be necessary for an orbital of the central atom in R to overlap with atomic orbitals of both the carbon atoms in the transition state. With elements of the first row in the periodic table, viz. C, H, O, N, the only possible orbitals are axially or centrally symmetrical (*s* and *p* orbitals) and cannot overlap efficiently in two directions less than 180° apart. This is shown very clearly by the great decrease in the rate of replacement reactions involving such atoms when a linear configuration of the transition state is sterically hindered (pp. 76, 205). If the classical mechanism were correct, rearrangements would occur only with considerable difficulty; but all the available evidence suggests that the rearrangements of carbonium ions are extremely rapid, and must therefore have unusually small activation energies.

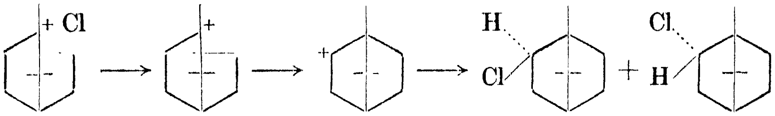
A satisfactory alternative interpretation has recently been given.† Removal of an R^+ cation from the reactant $\overset{\overset{R}{|}}{C}\text{—}\overset{+}{C}$ would leave a normal olefine. Now the R^+ cation will have a sextet of electrons on its central atom and should be a most powerful cationoid reagent; it should therefore readily form a π-complex with the olefine, being held to its π-electrons by a molecular bond. Such a π-complex should be comparable in stability to the original carbonium ion, so that rearrangement by the route



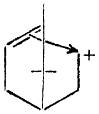
$$\overset{\overset{R}{|}}{C}\text{—}\overset{+}{C} \rightarrow \overset{\overset{R^+}{\uparrow}}{C{=}C} \rightarrow \overset{+}{C}\text{—}\overset{\overset{R}{|}}{C}$$

may require very little, if any, activation energy.

Definite evidence for such an intermediate is provided by the camphene hydrochloride rearrangement mentioned earlier. This reaction gives only *iso*-bornyl chloride, although if the cation rearranged completely before combining with the chloride anion, a mixture of bornyl and *iso*-bornyl chlorides would be expected:



If the intermediate ion is actually a π-complex,



attack by the anion should occur at the opposite side of the double bond from the molecular bond (cf. *trans* addition to olefines, p. 141), giving only one isomer.

The intermediate cation can in general give rise to more than one reaction product; thus *iso*-butyl chloride with aluminium chloride might give any of the isomeric butyl chlorides by the following rearrangements of the intermediate cation:

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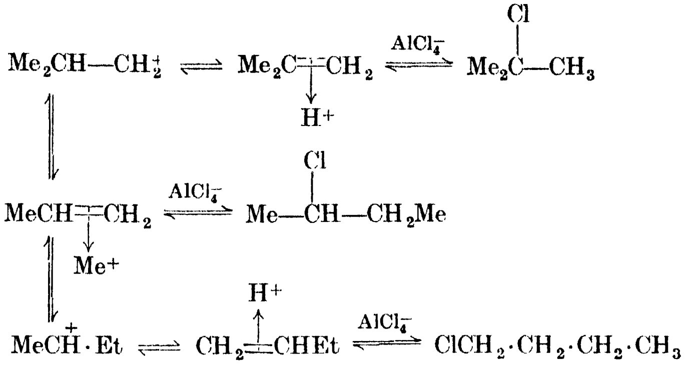
† Dewar, *J.C.S.* 1946, 406.

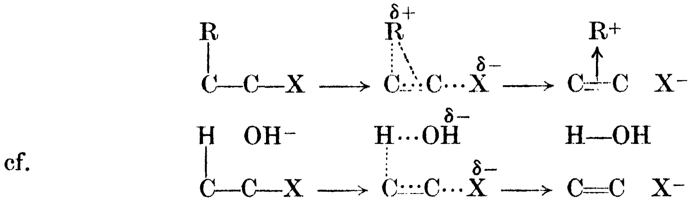
$$\mathrm{Me_2CH{-}CH_2Cl + AlCl_3 \rightleftharpoons Me_2CH{-}CH_2^+ + AlCl_4^-}$$



It seems very likely that the interconversion of π-complexes and normal cations is extremely rapid, so that the cation is in a state of dynamic equilibrium between all its possible isomers. Although there is no direct evidence for the correctness of these assumptions, they do enable us to explain in detail all the facts known about carbonium ion rearrangements and also, as we shall see, all the other known rearrangements of aliphatic compounds.

Effects of structure

The rate-determining step in all these rearrangements seems to be the preliminary ionization, the intermediate cation rearranging very rapidly. The rate of reaction will be increased by negative substituents which will facilitate ionization, just as in a normal $-S_1$ replacement. However, in most cases it is likely that the cation rearranges to a π-complex during the actual ionization process; the transition state for ionization will therefore resemble that of an elimination rather than a replacement, and should be stabilized by negative groups attached to either the α or the β carbon:



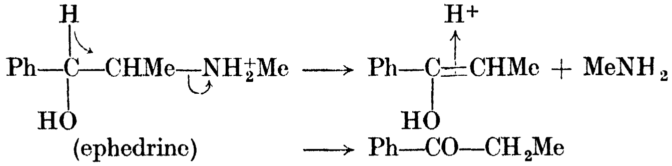
Furthermore, the stability of the π-complex will increase with the cationoid activity of the migrating cation. We may therefore conclude that

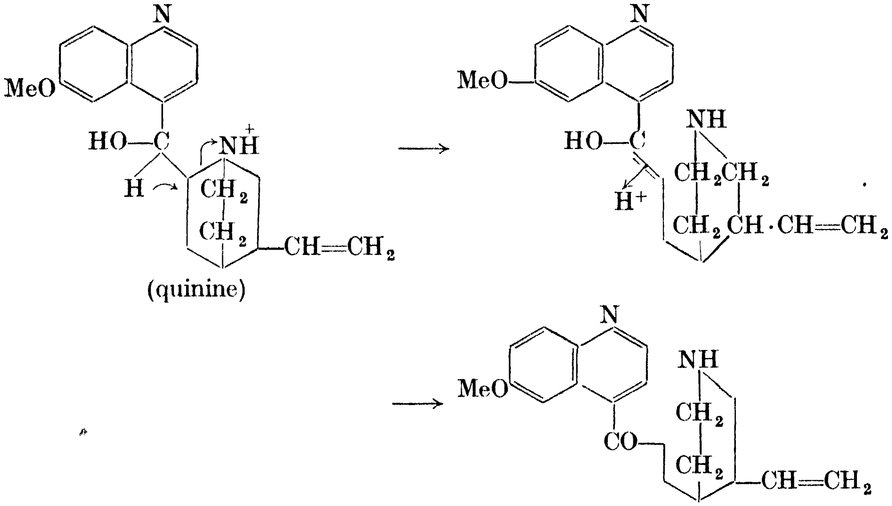
(1) the rate of rearrangement will be increased by negative substituents at the point of ionization or on the adjacent carbon from which migration occurs;

(2) groups migrate more readily, the more positive they are, since the energy of the transition state is less the more positive the migrating group.

Very few data are available to test these conclusions. The effect of

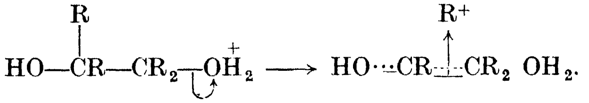
E-substituents on the rate of reaction is, however, very well shown in the hydramine fission. This reaction is a special case of the pinacol rearrangement whereby a β-aminoalcohol is converted by acid to a ketone and an amine or ammonia; during the reaction a hydrogen atom migrates. The hydramine fission only occurs under normal conditions if an aromatic group is attached to the carbon β to nitrogen, where it can conjugate with the double bond in the π-complex intermediate. Several alkaloids undergo the reaction readily, e.g. ephedrine and quinine:


$$\mathrm{Ph{-}\underset{HO}{\overset{H}{C}}{-}CHMe{-}\overset{+}{N}H_2Me \longrightarrow Ph{-}\underset{HO}{\overset{H^+}{C}}{=}CHMe + MeNH_2 \longrightarrow Ph{-}CO{-}CH_2Me}$$



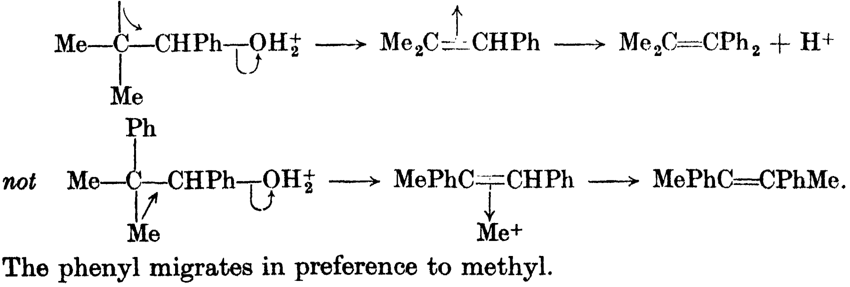
In the isomerization of alkyl halides by aluminium chloride, the equilibrium concentrations of the various isomers will depend on their relative heats of formation. Now the C—hal bond is highly polar, the carbon being the positive end of the dipole; an alkyl halide will therefore be stabilized by negative substituents α to halogen. Therefore in a series of isomeric halides, the heats of formation (i.e. the stability) should fall in the order *tert*-halide > *sec*-halide > *prim*-halide; and so at equilibrium *tert*-halides should be favoured. This is seen very clearly in the butyl chlorides where *tert*-butyl chloride predominates at equilibrium. In condensed-ring systems the position may be more complex, ring-strain and entropy effects becoming more important; as is the case with camphene hydrochloride, a *tert*-halide, which is readily converted to *iso*-bornyl chloride, a *sec*-halide. The intermediate cations probably exist mainly as π-complexes. The reaction of such a π-complex with an anion resembles the second stage in the addition of halogen to an olefine (p. 143); the anion will therefore add to the more substituted end of the double bond in the π-complex. Since, moreover, π-complexes are stabilized by negative groups conjugated with the double bonds in them, and by positiveness of the cation attached to the double bond, the most stable π-complexes in the equilibrium mixture of cations from an alkyl halide will be those where the maximum number of alkyl groups is attached to the double bond and the cation is H^+. Thus the most stable butyl cation is the π-complex $\mathrm{Me_2C\overset{\overset{H^+}{\uparrow}}{=}CH_2}$ and since this will react preferentially at the more substituted end of the double bond, it is easy to understand why *tert*-butylbenzene is the main product from the reaction of benzene with any butyl halide and aluminium chloride, or any butanol and sulphuric acid.

Since the first step in these reactions is the formation of a carbonium ion, they must occur only as alternatives to the normal modes of reaction of such ions (replacements and elimination). The electronic features favouring rearrangement are the same as those favouring $-S_1$ eliminations (p. 112), that is, negative substituents on either of the two relevant carbon atoms. Rearrangement will be favoured by conditions which favour $-S_1$ reactions in general, and it will also be favoured by the presence of positive groups on the β-carbon since these form the most stable π-complexes and can migrate most readily. These conclusions are supported by the qualitative evidence available. Thus the pinacol-type rearrangements take place with exceptional ease, the π-complex (and the transition state for its formation) being stabilized by the $-E$ effect of the second hydroxyl:



$$\mathrm{HO{-}\overset{R}{\overset{|}{C}}R{-}CR_2{-}\overset{+}{O}H_2 \longrightarrow HO\cdots CR\overset{\overset{R^+}{\uparrow}}{\cdots}CR_2\ OH_2}.$$

The case of migration ('migratory aptitude') increases in the order alkyl $<$ H $\sim$ aryl $<$ aryl with positive substituents, that is, in the order of cationoid activity of the groups. (Migration of hydrogen cannot as a rule be distinguished from simple $-S_1$ elimination and both reactions may well take place through similar π-complexes. In this sense the migratory aptitude of H is about the same as Ph.) A simple illustration† of the kind of evidence available is:



$$\mathrm{Me{-}\overset{Ph}{\underset{Me}{C}}{-}CHPh{-}OH_2^+ \longrightarrow Me_2C\overset{\overset{Ph^+}{\uparrow}}{=}CHPh \longrightarrow Me_2C{=}CPh_2 + H^+}$$

$$\textit{not}\quad \mathrm{Me{-}\overset{Ph}{\underset{Me}{C}}{-}CHPh{-}OH_2^+ \longrightarrow MePhC\underset{\underset{Me^+}{\downarrow}}{=}CHPh \longrightarrow MePhC{=}CPhMe.}$$

The phenyl migrates in preference to methyl.

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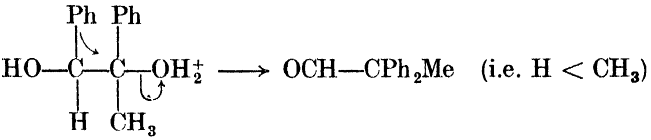
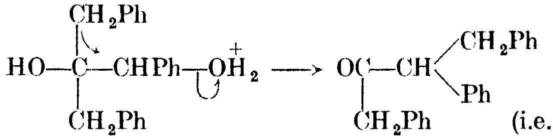
† Lévy, *Bull. Soc. Chim.* 1921 (iv), **29**, 878.

The pinacol-pinacoline rearrangement differs from the other carbonium ion rearrangements in that the preliminary ionization may occur in two different ways. In an unsymmetrical pinacol, the hydroxyl with the most negative groups in the α-position will appear as carbonyl in the product. The observed effect of substituents in increasing the ease of ionization follows their known order of anionoid reactivity, viz. H < alkyl < aryl < negatively substituted aryl. This is illustrated by the following examples:

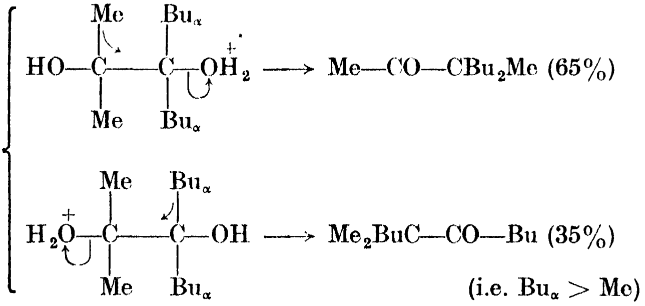


$$\mathrm{HO{-}C(Ph)(H){-}C(Ph)(CH_3){-}OH_2^+} \longrightarrow \mathrm{OCH{-}CPh_2Me} \quad (\text{i.e. } \mathrm{H} < \mathrm{CH_3})$$



$$\mathrm{HO{-}C(CH_2Ph)_2{-}CHPh{-}\overset{+}{O}H_2} \longrightarrow \mathrm{OC(CH_2Ph){-}CH(CH_2Ph)(Ph)}$$

(IV) (i.e. $\mathrm{PhCH_2} \ll \mathrm{Ph}$)



$$\mathrm{HO{-}C(Me)_2{-}C(Bu_\alpha)_2{-}\overset{+}{O}H_2} \longrightarrow \mathrm{Me{-}CO{-}CBu_2Me}\ (65\%)$$

$$\mathrm{H_2\overset{+}{O}{-}C(Me)_2{-}C(Bu_\alpha)_2{-}OH} \longrightarrow \mathrm{Me_2BuC{-}CO{-}Bu}\ (35\%) \quad (\text{i.e. } \mathrm{Bu_\alpha} > \mathrm{Me})$$

Incidentally the dibenzylphenylglycol (IV), if initially optically active, gives an active ketone on rearrangement, though much racemization also takes place.† This implies that the rearrangement to the π-complex must occur almost immediately after ionization of the hydroxyl.

The reverse pinacol-pinacoline rearrangement

The isomerization of alkyl halides by aluminium halides is completely reversible; so too must be the other rearrangements of carbonium ions. However, since rearrangement competes successfully with normal replacement or elimination only when the rearranged cation is more stable than the parent ion, the reverse reaction will occur only with difficulty. For instance, the reverse pinacol-pinacoline rearrangement should be catalysed by acids, and so the pinacol-pinacoline reaction should lead to an equilibrium:

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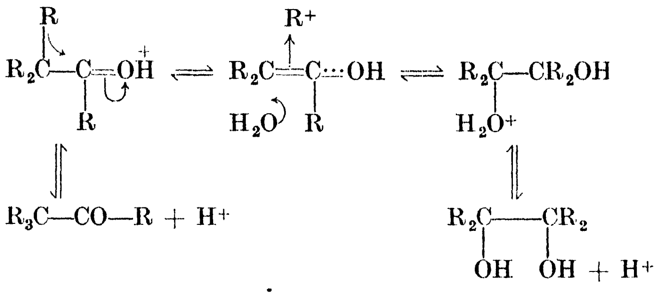
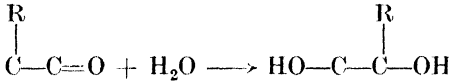
† Roger and McKenzie, *Ber.* 1929, B **62**, 272.

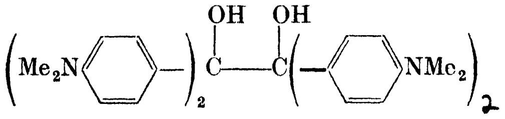


Examination shows that the overall reaction may be written formally as:

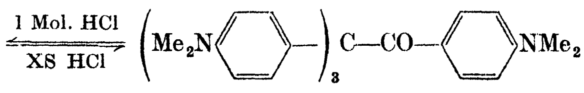


$$\overset{R}{\overset{|}{C}}-C=O + H_2O \longrightarrow HO-C-\overset{R}{\overset{|}{C}}-OH$$

The reactants and products differ only in that a C=O bond in the former has been replaced by two C—O bonds in the latter. From the bond-energy table it is therefore seen that the ketone should be formed exothermically (about 10 Cals.), and should be favoured at equilibrium. Hence the reverse pinacol-pinacoline rearrangement should be observed only when the pinacol is either stabilized in some way, or removed as soon as it is formed. Only one example is known,† illustrating the latter case. *Tetrakis*-(*p*-dimethylaminophenyl)glycol (V) is converted by an excess of strong acid into the pinacoline (VI); but the latter is reconverted to (V) by weak acids or by exactly one mole of strong acid. Evidently the glycol is converted to the mesomeric ion (VII) as soon as it is formed and is thus removed from the system. Excess strong acid converts (VII) into the non-mesomeric salt (VIII) which easily adds water to regenerate a salt of the glycol (V), and hence gives the parent pinacoline.



(V)



(VI)

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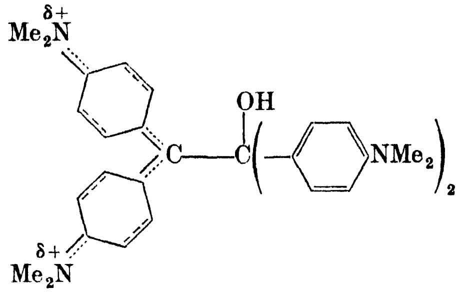
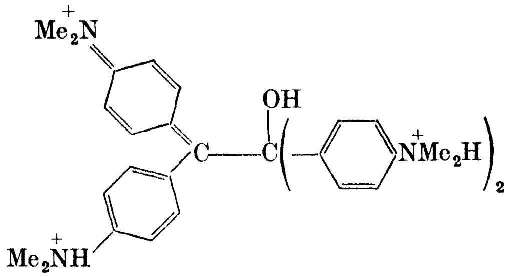
† Madelung and Oberwegner, *Ber.* 1927, B **60**, 2469.



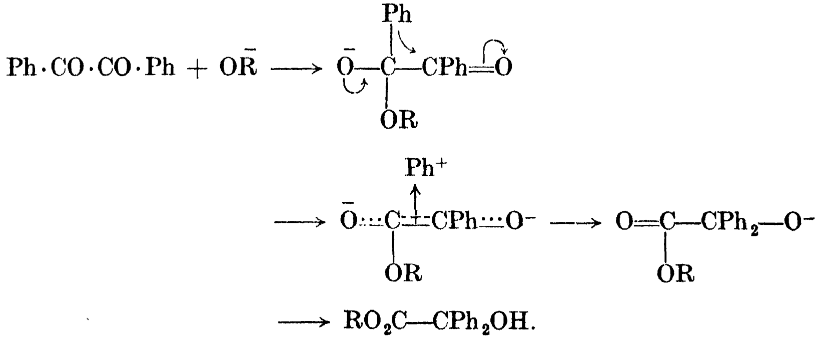
(VII)



(VIII)

The benzilic acid rearrangement

Although no simple cases are known where mesomeric stabilization of a pinacol makes possible its preparation from a pinacoline, the benzilic acid rearrangement provides a close analogy. The first step must be an addition of alkali to the benzil, since ethoxide ion can certainly give an addition product with benzil and the latter rearranges to ethyl benzilate; the only reasonable mechanism seems to be:



$$\mathrm{Ph{\cdot}CO{\cdot}CO{\cdot}Ph} + \mathrm{O\bar{R}} \longrightarrow \bar{\mathrm{O}}-\underset{\underset{\displaystyle \mathrm{OR}}{|}}{\overset{\overset{\displaystyle \mathrm{Ph}}{|}}{\mathrm{C}}}-\mathrm{CPh{=}O}$$

$$\longrightarrow \bar{\mathrm{O}}\cdots\underset{\underset{\displaystyle \mathrm{OR}}{|}}{\overset{\overset{\displaystyle \mathrm{Ph}^{+}}{\uparrow}}{\mathrm{C}}}\cdots\mathrm{CPh}\cdots\mathrm{O}^{-} \longrightarrow \mathrm{O}{=}\underset{\underset{\displaystyle \mathrm{OR}}{|}}{\mathrm{C}}-\mathrm{CPh_2}-\mathrm{O}^{-}$$

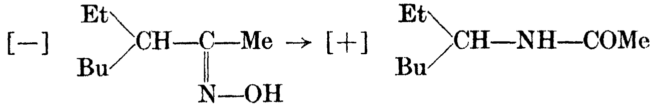
$$\longrightarrow \mathrm{RO_2C}-\mathrm{CPh_2OH}.$$

The π-complex should be relatively stable since two very strongly —E groups ($-\bar{\mathrm{O}}$) are conjugated with the double bond in it. The product, though formally analogous to a pinacol, is stabilized to the extent of the carboxyl resonance energy, and so the reverse reaction should occur only with difficulty. In any case the proportion of acid existing in the form appropriate to the reverse reaction $(HO_2C{-}CPh_2{-}\bar{O})$ would be infinitesimal, since the carboxyl group is enormously more acidic than an alcoholic hydroxyl.

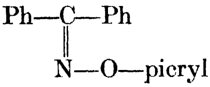
The Beckmann rearrangement

According to the latest evidence, the Beckmann rearrangement is closely analogous to the carbonium ion rearrangements, but the migration takes place not from carbon to carbon, but from carbon to nitrogen. The essential points may be summarized.

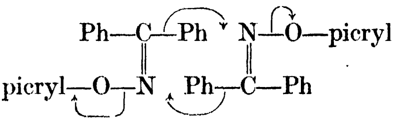
1. The rearrangement is intramolecular, asymmetric groups migrating without loss of optical activity,† e.g.



2. The rearrangement of benzophenone oxime picryl ether (IX) is unimolecular‡ refuting mechanisms such as (X).



(IX)



(X)

3. The group which migrates to nitrogen is the one *trans* to the hydroxyl in the parent oxime.§

4. Oximes themselves rearrange very slowly, if at all, with acids; but their esters with strong acids rearrange readily. Moreover, the rate of rearrangement of such esters varies with the strength of the acid; thus in 10 minutes at 60° the following fractions of various esters of benzophenone oxime rearrange.‖

Acid	$PhSO_3H$	$PhCOOH$	$ClCH_2COOH$	CH_3COOH
Per cent. conversion . .	100	93	61	0

Furthermore, the rate of rearrangement of benzophenone oxime picryl ether is much greater in polar solvents, the rates in CCl_4, benzene, and $CH_2Cl{\cdot}CH_2Cl$ at 60° being in the ratio†† 0·15 : 1 : 35. These results can mean only one thing, that the rate-determining step in the reaction is the ionization of the oxime, ether, or ester. The *trans* migration must then imply that rearrangement accompanies ionization in a single adiabatic process, the reaction resembling the internal $-S_2$ displacement of bromine in β-acetoxyalkyl bromides (p. 78):

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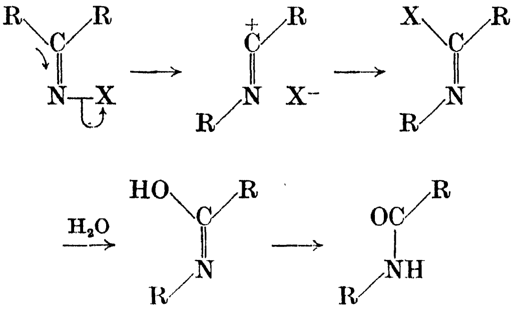
† Kenyon and Young, *J.C.S.* 1941, 263.

‡ Kuhara and Todo, *Mem. Coll. Sci. Kyoto Imp. Univ.* 1910, **2**, 387.

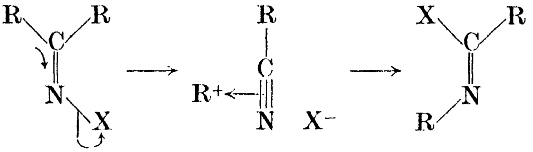
§ For a general survey see Brynmor Jones, *Chem. Rev.* 1944, **35**, 335.

‖ Kuhara, *The Beckmann Rearrangement*, Tokyo, 1926.

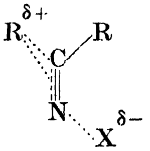
†† Chapman, *J.C.S.* 1934, 1550. The rate in CCl_4 is also increased by addition of small quantities of polar substances such as MeCN, $MeNO_2$.



The simplest interpretation of these results is that a π-complex mechanism is again operating, viz.



The *trans* migration would follow from steric considerations, and from the fact that in the transition state one lobe of the nascent π-bond is used to bind the departing X⁻ ion:



The other π-orbital plays no part in the reaction, since it is perpendicular to the one formed during reaction and therefore is unable to overlap with orbitals on the relevant atoms or groups.

The rate of the reaction depends only on the rate of initial ionization, and therefore increases with negativity of the groups in the parent oxime. This relation was established quantitatively by Chapman and Fidler,† who showed that *p*-Cl reduced, and *p*-Me increased, the rate of rearrangement of benzophenone oxime picryl ethers.

The rearrangement of oximes by phosphorus pentachloride does not differ from those of their esters and ethers; it has been proved‡ that similar ethers are intermediates in the phosphorus pentachloride reaction, the mechanism being:

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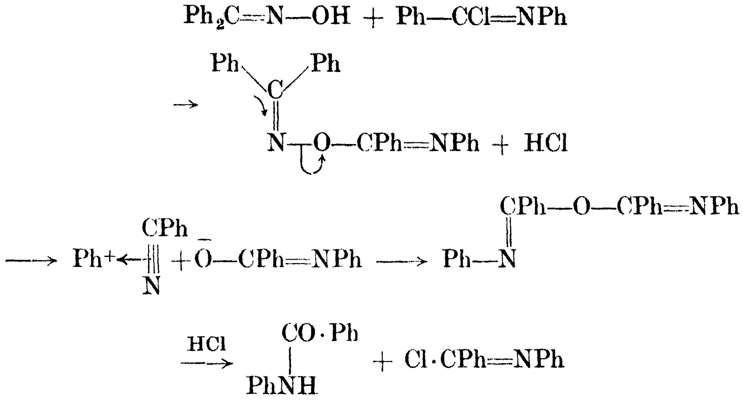
† *J.C.S.* 1936, 448.

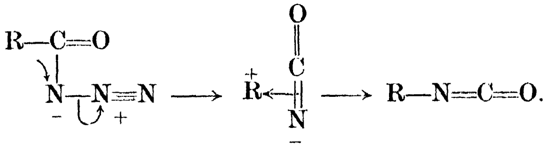
‡ Chapman, *J.C.S.* 1935, 1223, 1226.



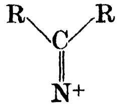
The resulting amide can give yet more iminochloride with the phosphorus pentachloride; consequently the reaction is autocatalytic.

Related non-ionic rearrangements (Hofmann, Curtius, etc.)

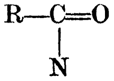
A series of rearrangements are known which are clearly analogous to the Beckmann and carbonium ion rearrangements, but in which the intermediate is uncharged. For instance, acid azides break down on heating into *iso*-cyanates and nitrogen, a reaction best represented:



The relation to the earlier rearrangements is more clearly seen if we consider the classical formulae for the imaginary precursors of the π-complexes:

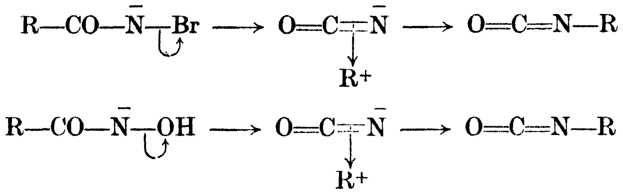


(XI)



(XII)

In each case nitrogen has a sextet of electrons, that is, it has potentially an empty p-orbital. Removal of the migrating group R as R^+ would leave an unshared pair of electrons on the carbon adjacent to nitrogen; these can form a dative π-bond with the adjacent nitrogen, and to this π-bond R^+ can be attached to form a π-complex. The same process is possible in the case of both (XI) and (XII), so the Curtius and Beckmann rearrangements presumably have an analogous mechanism. The Hofmann and Lössen rearrangements presumably pass through a π-complex similar to that formed in the Curtius rearrangement.



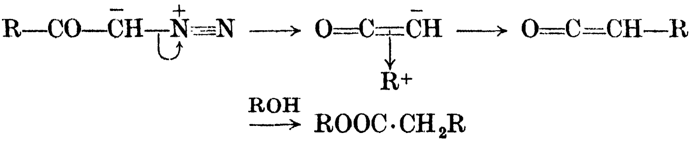
$$R{-}CO{-}\bar{N}{-}Br \longrightarrow O{=}\underset{\underset{R^+}{\downarrow}}{C}{=}\bar{N} \longrightarrow O{=}C{=}N{-}R$$

$$R{-}CO{-}\bar{N}{-}OH \longrightarrow O{=}\underset{\underset{R^+}{\downarrow}}{C}{=}\bar{N} \longrightarrow O{=}C{=}N{-}R$$

It is known that these rearrangements are intramolecular, since asymmetric groups retain their configuration during migration.† This result is well explained by the π-complex theory since the asymmetric group remains attached throughout to the rest of the molecule by a single bond. The fact that in the intermediate π-complex the other end of the bond is a molecule and not an atom is irrelevant to the stereochemistry of the migrating group.

The rate of rearrangement depends on the rate of removal of the nitrogen, bromine, or hydroxyl, a process equivalent to ionization. As in the Beckmann rearrangement, this rate will be determined by the negativity of the group R in the initial compound $R{-}CO{-}\bar{N}\cdot X$. Hauser and Renfrow‡ have shown that this relation holds for a large number of *m*- and *p*-substituted benzoyl derivatives, the rates obeying Hammett's law (p. 172).

The Arndt–Eistert rearrangement of diazoketones resembles formally the rearrangements of acyl azides, and very probably takes place by a similar mechanism.



$$R{-}CO{-}\bar{C}H{-}\overset{+}{N}{\equiv}N \longrightarrow O{=}\underset{\underset{R^+}{\downarrow}}{C}{=}\bar{C}H \longrightarrow O{=}C{=}CH{-}R$$

$$\xrightarrow{ROH} ROOC\cdot CH_2R$$

The ketene reacts with water, alcohol, or ammonia to give the observed reaction product. There is no direct proof that ketenes are intermediates in the reaction. It has, however, been shown that asymmetric groups migrate with retention of configuration ;§ and also that the carboxyl group in the final acid is derived from the original carbonyl, since the diazoketone from benzoic acid, where the COOH group has been enriched in the carbon isotope C^{13}, gives phenylacetic acid where the C^{13} is all contained in the carboxyl.‖ These results are difficult to explain in other terms.

$$Ph\cdot\overset{*}{C}O\cdot CHN_2 \rightarrow Ph\cdot CH_2\cdot\overset{*}{C}OOH$$

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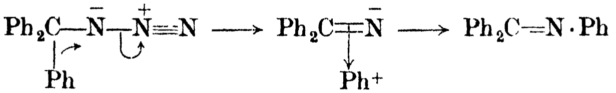
† Arcus and Kenyon, *J.C.S.* 1939, 916; Kenyon and Young, ibid. 1941, 263. Wallis et al., *J.A.C.S.* 1931, **53**, 2787; 1933, **55**, 1701; *J. Org. Chem.* 1942, **7**, 261.

‡ *J.A.C.S.* 1937, **59**, 121.

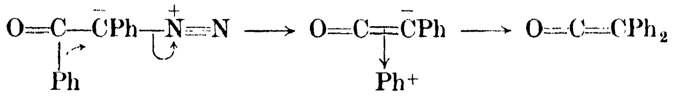
§ Lane, Willenz, Weissberger, and Wallis, *J. Org. Chem.* 1940, **5**, 276; Lane and Wallis, *J.A.C.S.* 1941, **63**, 1674.

‖ Huggett, Arnold, and Taylor, *J.A.C.S.* 1942, **64**, 3043.

Two further rearrangements, which are probably of the same type, are:



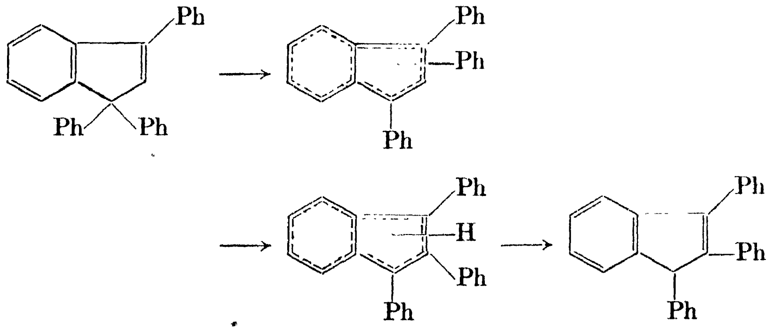
$$\mathrm{Ph_2\underset{Ph}{C}-\overset{-}{N}-\overset{+}{N}\equiv N \longrightarrow Ph_2C\!=\!\underset{Ph^+}{\bar{N}} \longrightarrow Ph_2C\!=\!N\cdot Ph}$$



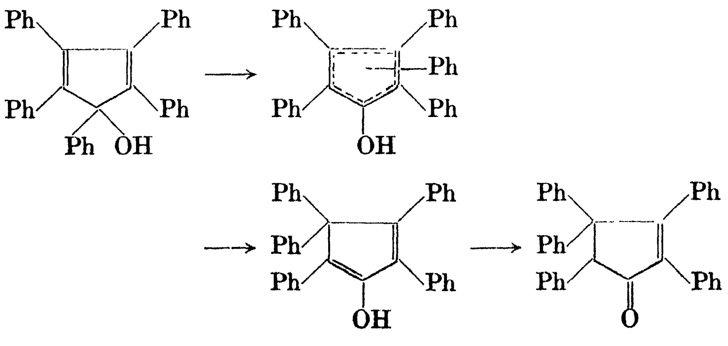
$$\mathrm{O\!=\!\underset{Ph}{C}-\overset{-}{C}Ph-\overset{+}{N}\equiv N \longrightarrow O\!=\!\underset{Ph^+}{C}\!=\!\bar{C}Ph \longrightarrow O\!=\!C\!=\!CPh_2}$$

Other aliphatic rearrangements

One other minor class of rearrangements may be mentioned. There is no evidence at all for their mechanism, but it seems likely that π-complex intermediates are involved. Apparently the parent molecule could theoretically split into a cation and a mesomeric anion; these can form a π-complex, and so the molecule can isomerize to a π-complex and thus pass into an isomer of the starting material. The reaction resembles prototropic tautomerism except that the ions remain combined throughout. A simple example is the rearrangement† of 1:1:3-triphenylindene to 1:2:3-triphenylindene, which is best represented:



Similar again is the rearrangement‡ of pentaphenyl*cyclo*pentanol:



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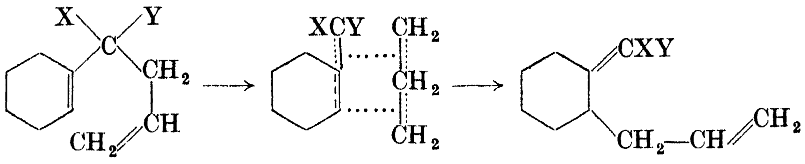
† Koelsch and Johnson, *J.A.C.S.* 1943, **65**, 567.

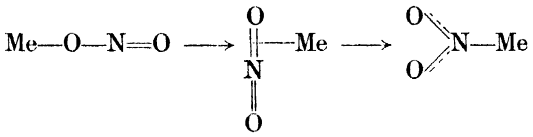
‡ Allen and Van Allan, ibid. 1943, **65**, 1384; 1944, **66**, 7.

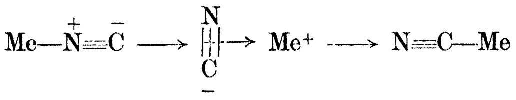
and the rearrangements of allyl derivatives.† For example:

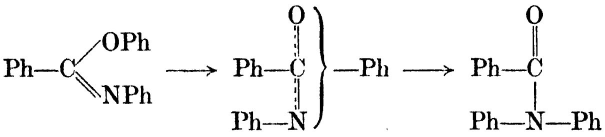


X, Y = CN or COOEt

In these rearrangements both components are mesomeric, and the molecular bond probably links the whole mesomeric systems together as indicated in the last example. Incidentally mesohydric tautomerism (p. 193) is a special case of this kind of reaction where the migrant is hydrogen; and the isomerization of *iso*-cyanides to cyanides, nitrites to nitrocompounds, iminoethers to amides, cyanates to isocyanates, etc., are probably also of the same type. For example:







These rearrangements are really intermediate in type between the other aliphatic rearrangements and those of aromatic compounds which will be discussed in the following chapter.

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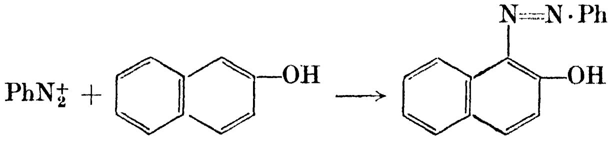
† Cope et al., *J.A.C.S.* 1940, **62**, 441; 1941, **63**, 1843.

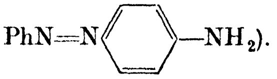
CHAPTER XI

MOLECULAR REARRANGEMENTS: AROMATIC SERIES

A NUMBER of N-substituted anilines rearrange on treating with acid under suitable conditions to give *ortho-* or *para*-substituted anilines. The migrating group may be halogen, alkyl, OH, NO_2, NH_2, NHAr, acyl, or $-N{=}N\cdot Ar$. The mechanism of these reactions is complex and has only recently received a satisfactory interpretation. The situation is obscured by the difficulty of establishing whether or not the rearrangements are truly intra-molecular. Those of diazoaminobenzene derivatives, $Ar\cdot N{=}N\cdot NH\cdot Ar$, almost certainly are not, since in presence of a better coupling agent than the parent amine (e.g. β-naphthol), the only product is an azo-derivative of the foreign molecule,[†] e.g.

$$\mathrm{Ph\cdot N{=}N\cdot NHPh + HCl \rightarrow PhN_2^+\ Cl^- + PhNH_2}$$



(and not $\mathrm{PhN_2^+ + PhNH_2 \rightarrow}$ ).

The reactions can be divided into three groups. In the first, no migration to a foreign nucleus has ever been observed and the reactions are unquestionably intramolecular; phenylhydroxylamine and hydrazobenzene derivatives are examples.[‡] In the second, migration to foreign nuclei may occur, but the rearrangements seem nevertheless to be intramolecular; the N-nitraniline, haloacetanilide, and Hofmann rearrangements are examples. The third group of intermolecular or 'pseudo' rearrangements is illustrated by diazoaminobenzene. The evidence for mechanism in these reactions may be summarized.

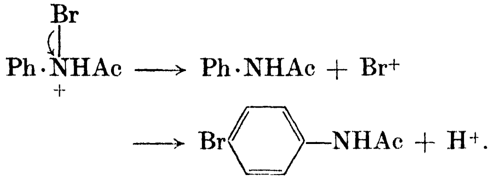
Haloacylanilide rearrangement

This reaction has been studied in detail by Bell and his collaborators.[§] The rearrangements of N-bromacetanilide and N-iodoformanilide in aprotic solvents are acid-catalysed and unimolecular, and the kinetics prove that the rate-determining step is a transfer of a proton from the catalyst to the anilide to form a salt; the salt rearranges practically instantaneously. The reaction cannot take place by intermediate liberation of free halogen and acylanilide followed by halogenation, since the concentration of free halogen present during reaction is too small to account for the observed rate. The only other possible intermolecular mechanism would be the separation of free halogen cations from the intermediate salt, viz.:

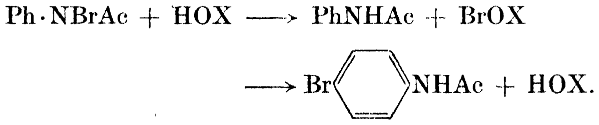
[†] Nietzki, *Ber.* 1877, **10**, 662; Rosenhauer and Unger, ibid. 1928, **61**, 392; Kidd, *J. Org. Chem.* 1937, **2**, 198.

[‡] Ingold and Kidd, *J.C.S.* 1933, 984.

[§] *Proc. Roy. Soc.* 1934, A **143**, 377; 1935, A **151**, 211; *J.C.S.* 1936, 1154, 1520; 1939, 1774.



However, other evidence shows that the Br^+ ion must be an exceedingly powerful cationoid reagent, and the almost quantitative yield of *p*-bromacetanilide obtained when the reaction is carried out in benzene derivatives shows that such a cation cannot possibly be set free as an intermediate since it would attack the solvent. Israel, Tuck, and Soper† found that if the rearrangement were carried out in anisole, partial bromination of the solvent did take place, but *p*-bromacetanilide was still formed in large amount. They held that this observation showed the reaction to be intermolecular and suggested that a reactive acyl hypohalite was formed as an intermediate.



This mechanism does not account for the quantitative relation observed by Bell between rate of reaction and acid strength of the catalyst. Moreover, in anisole the ionic mechanism should lead almost exclusively to halogenation of the solvent, so the evidence actually makes the intermediate formation of a halide cation very unlikely. The most satisfactory explanation seems to be that the rate-determining step is a proton transfer to the N-haloacylanilide; the cation then undergoes a true rearrangement to *p*-haloacylanilide. In the intermediate stages of this rearrangement the halogen is weakly bound and can substitute reactive foreign molecules such as anisole.

The nitraniline rearrangement

This reaction has been studied in considerable detail by Orton and his collaborators.‡ The reaction is acid-catalysed, like the haloacylanilide rearrangement, but the main product is an *o*-nitraniline. Since aniline derivatives give mainly *p*-nitranilines with nitric acid, it seems likely that the rearrangement is intramolecular and does not take place by fission to nitric acid and aniline. As in the haloacylanilide rearrangement, the migrating group can be transferred to another nucleus, but again it seems likely that transfer takes place from a rearrangement intermediate and not by fission of the nitraniline. In this case ionization to free NO_2^+ cannot possibly occur since this ion is known to be extremely reactive, and would at once react with most solvents, including water.

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† *J.C.S.* 1945, 547.

‡ *Brit. Assoc. Reports*, 1912, 117; *J.C.S.* 1929, 915.

The Hofmann rearrangement

Here again transfer of alkyl to foreign nuclei has been observed, but since the main product is a simple C-alkyl derivative of the parent aniline, and since such a derivative would be substituted more rapidly than the parent aniline by cationoid reagents, it seems certain that the reaction must be essentially intramolecular. Olefines cannot be intermediates since N-methylanilines rearrange, and since rearrangement takes place at high temperatures in open vessels where any olefine would distil out of the system, and since olefines do not readily react with anilines under the conditions used. Nor can alkyl cations formed by the reaction

$$\mathrm{Ph}\cdot\overset{+}{\mathrm{N}}\mathrm{R_2H} \rightarrow \mathrm{PhNHR} + \mathrm{R}^+$$

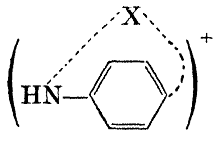
be intermediates, since then polyalkylanilines would be the main products of reaction (the alkylation products of the aniline would react more rapidly with R^+ than would the parent base).

Phenylhydroxylamine rearrangement

As already mentioned, the acid-catalysed rearrangement of phenylhydroxylamine to *p*-aminophenol is almost certainly intramolecular, since no migration of hydroxyl to other nuclei has been observed, nor is there any indication that hydrogen peroxide is formed when the reaction is carried out in water; HO^+ ions would certainly react with water to form $H_2O_2 + H^+$.

Mechanism of the rearrangements

From a classical point of view these rearrangements are very strange indeed. There seems little doubt that they are mainly, if not entirely intramolecular, and if so the migrating group must be attached in the transition state by partial bonds to two atoms nearly 5 A apart:

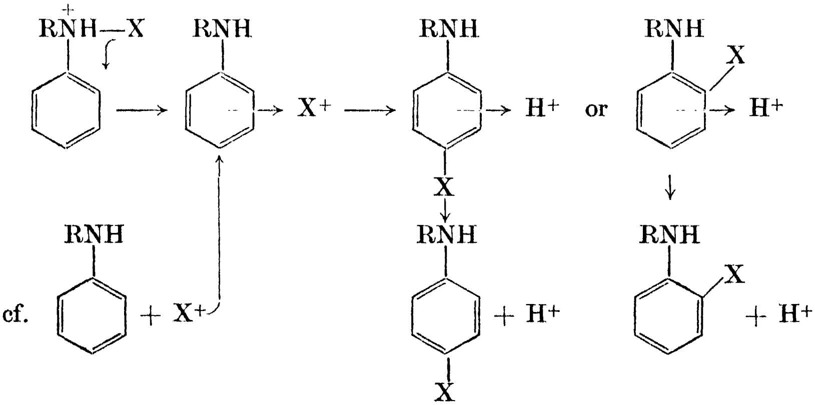


Such a transition state would be unstable and its heat of formation relatively high. Yet the main characteristic of these reactions is their extraordinary rapidity, N-bromacetanilide, for example, rearranging at measurable speed only under conditions such that the anilide accepts protons slowly; the actual cation must rearrange almost instantaneously and the activation energy for rearrangement must be small.

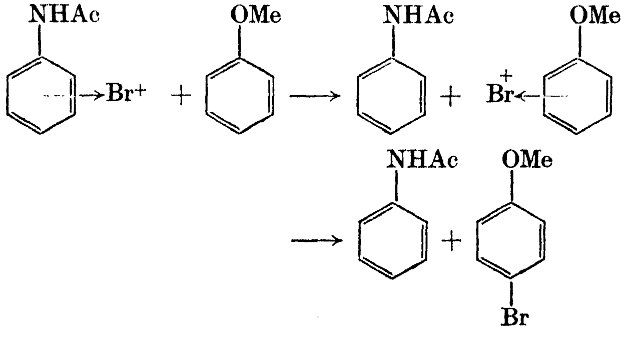
The only reasonable explanation seems to be that rearrangement proceeds through an intermediate π-complex, resembling the rearrangements discussed at the end of the last chapter. The rearrangement

$$\mathrm{Ph{\cdot}\overset{+}{N}HRX} \rightarrow \mathrm{X{\cdot}C_6H_4{\cdot}NHR} + \mathrm{H^+}$$

may be regarded as taking place by fission to X^+ and PhNHR, but the X^+ will have a sextet of electrons only, and can form a bond with the π-electrons of the aniline. Since the aniline π-orbitals cover the nitrogen atom as well as the nucleus, it is possible for the N—X link to pass into a molecular bond (Ph—N)—X without any change in the stereochemistry of the molecule. The group X can then migrate to the nuclear part of the π-orbital, remaining all the time linked by a molecular bond to the rest of the molecule. The resulting form of the π-complex will then be identical with the π-complex formed in cationoid substitution of the aniline by X^+, and the subsequent replacement of nuclear hydrogen will be the same in both reactions, i.e.



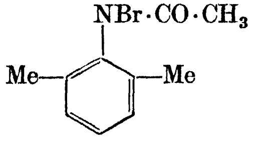
The intermediate π-complex will be a potential source of an X^+ cation, and in the presence of a reactive foreign nucleus, e.g. anisole, a transfer of X^+ can occur, for example:



It is therefore possible to explain these rearrangements very satisfactorily in terms of π-complex intermediates, and thereby also to establish their analogy to other rearrangements and to normal aromatic substitution. Furthermore, the differences between the various reactions, and the abnormal orientation of the product from N-nitraniline, can be explained. The stability of the π-complex will vary inversely with the stability of the free cation X^+. The diazonium cation will have little tendency to form a π-complex, being itself quite stable, and so diazoaminobenzene rearranges by fission and resynthesis (cf. the similar explanation of differences in orientation in substitution and diazo-coupling reactions, p. 171). The OH^+ and $PhNH^+$ cations must be very unstable, so phenylhydroxylamine and hydrobenzene (*vide infra*) rearrange intramolecularly and no transfer of the migrating group to a foreign nucleus has been observed. Finally, the cations NO_2^+, (hal)$^+$, and (alkyl)$^+$ are known in the form of salts or reaction intermediates. Their stability is small and therefore intramolecular rearrangement of the corresponding N-substituted anilines is possible, but the π-complex intermediates are nevertheless sufficiently unstable for the migrating group to be transferred to a reactive foreign nucleus.

Since the group X^+ has to pass round the ring from nitrogen to reach the *para*-position in the π-complex, a highly reactive X^+ may be removed on the way by replacing hydrogen from an *ortho*-position. Since NO_2^+ is a much more active substituting agent than (hal)$^+$ or (alkyl)$^+$, it is not surprising that the main product from N-nitraniline is *o*-nitraniline. With the other cations the π-complexes achieve the same statistical configuration that would arise in a normal π-complex substitution intermediate, and so the rearrangement product is mainly a *p*-substituted aniline, as is also the product from a normal substitution reaction (e.g. nitration).

An interesting test of the π-complex theory should be feasible. If the rearrangement depends on the ability of the N—X bond to pass over into a π-bond without change in molecular configuration, steric hindrance of the conjugation between nitrogen and the ring should reduce the rate of reaction. Thus 2:6-dimethyl-N-bromacetanilide



should rearrange only with difficulty by the intramolecular mechanism, since the π-orbitals of the ring will not extend to the nitrogen.

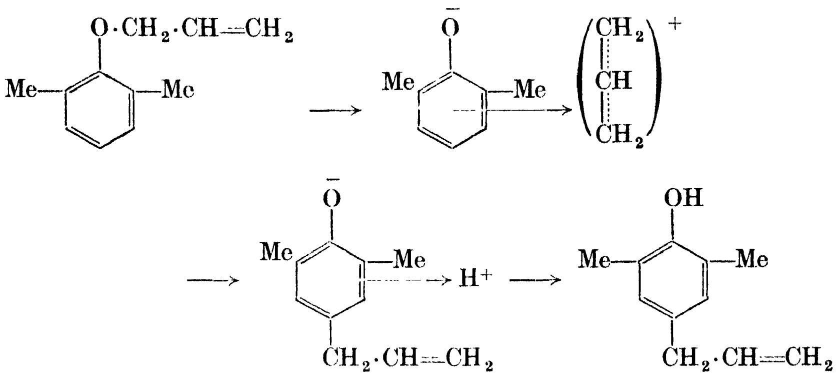
Other related rearrangements

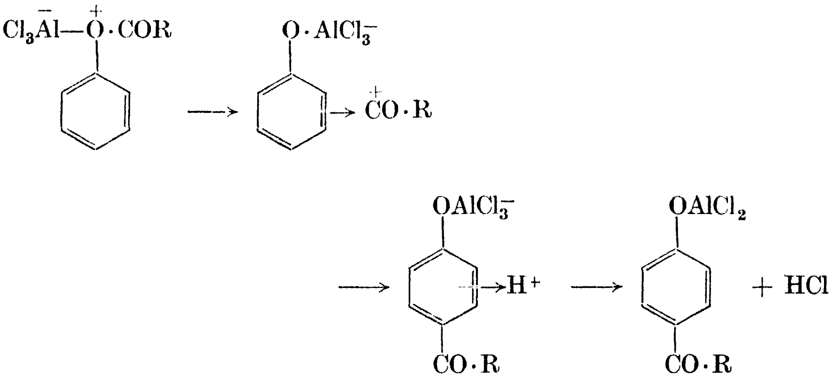
The *p*-Claisen rearrangement† of allyl ethers and the Fries rearrangement‡ of aryl esters with aluminium chloride may proceed through similar π-complexes. It is difficult to explain otherwise why either the α- or

† See Tarbell, *Organic Reactions*, **2**, 1.

‡ See Blatt, ibid. **1**, 342.

γ-carbon of the allyl group may be attached to the nucleus in different cases, or why Fries rearrangement of aryl esters gives better yields than Friedel–Craft acylation of the corresponding phenol (if fission to phenol and an acyl cation were the first step in the former reaction, both should give similar yields of hydroxyketone).





Another similar type of rearrangement is the migration of groups round a benzene ring under the influence of cationoid reagents. The simplest examples are certain acid-catalysed rearrangements where the most natural explanation would be that the acid brings about a reverse substitution of one of the groups in the ring, and this then resubstitutes in a different position. However, this explanation has been disproved in at any rate two cases. Firstly, the interconversion† of *o*- and *p*-toluene sulphonic acids certainly does not proceed by fission and resynthesis, nor by sulphonation followed by hydrolysis of one sulphonic acid group; for no disulphonic acid is found in the products and no *m*-toluenesulphonic acid, although the latter is always formed in the nitration of toluene. Moreover, *m*-toluenesulphonic acid is not rearranged by sulphuric acid.

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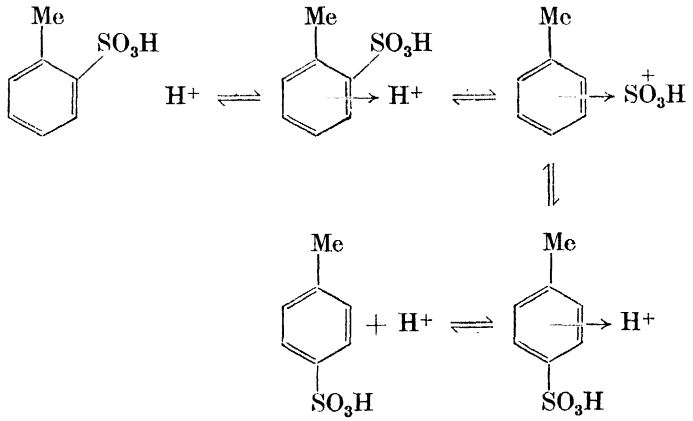
† Holleman and Callard, *Ber.* 1911, **44**, 2519.

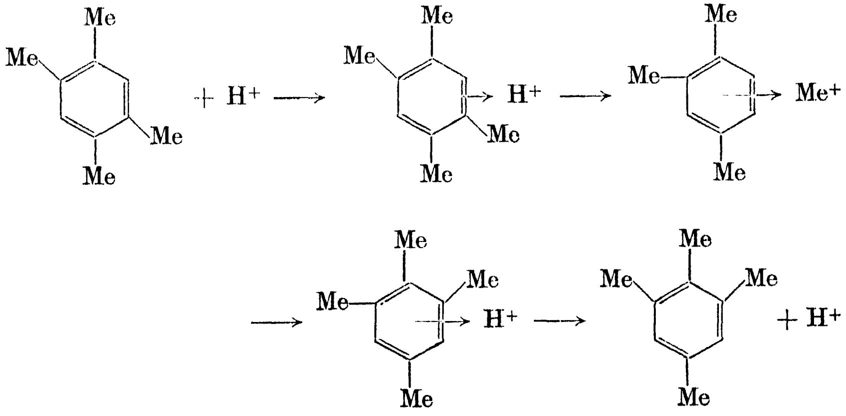
Secondly, it has been shown that in the Jacobson rearrangement† an alcohol or alkyl sulphate is not an intermediate; and the only other possible intermediate, an alkyl cation, would react at once under the operative conditions (aqueous or concentrated sulphuric acid) to form one of these compounds.

The most reasonable explanation seems to be that the reactions do take place by reverse substitution, but only to the extent of formation of the intermediate π-complex; namely:

(1)



(2)



In the latter case transfer of alkyl to a foreign nucleus does occur, but only to a small extent, and this we should expect from analogy with the Hofmann rearrangement. There is also evidence that sulphonation precedes rearrangement; this would also be easily intelligible if π-complex formation by H^+, and also displacement of alkyl by H^+, occurred with difficulty. The toluenesulphonic acid rearrangement shows that the HSO_3

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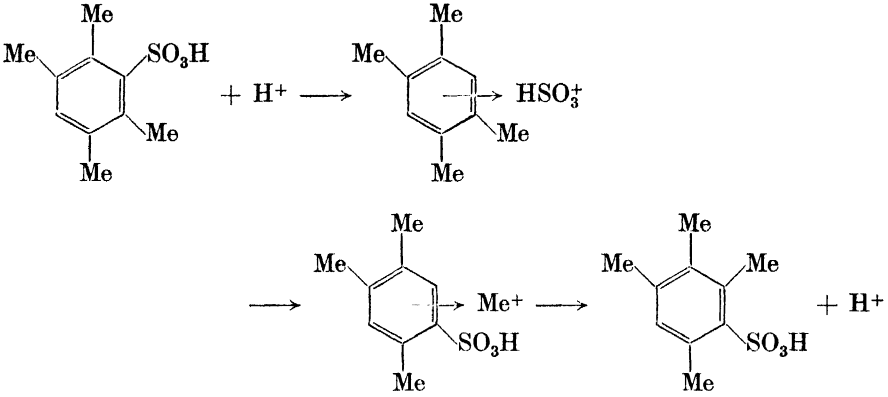
† See L. I. Smith, *Organic Reactions*, **1**, 370.

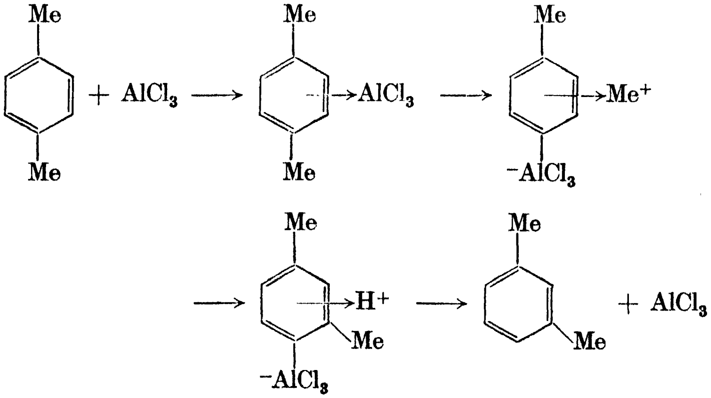
group is readily displaced by H^+, so the mechanism of the Jacobson rearrangement may really be of the type:



All the available evidence can be interpreted in this way.

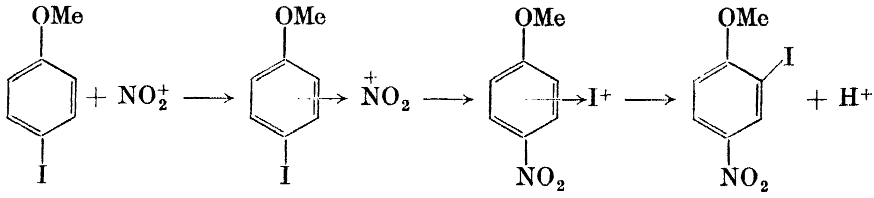
For these reactions to be possible the intermediate π-complex must be stabilized and the cationoid replacement of the migrating group activated by negative *o*- or *p*-substituents. Hence *m*-toluenesulphonic acid fails to rearrange.

The rearrangements of alkylbenzene derivatives by aluminium chloride, and the reverse Friedel–Craft reaction, are no doubt similar. Aromatic hydrocarbons are known to form coordination compounds with aluminium halides (p. 170) which must be π-complexes. Thus the rearrangement of *p*-xylene may be represented:



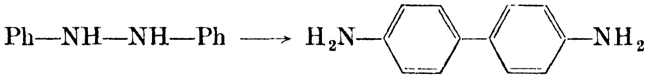
Another interesting rearrangement, probably intramolecular, was discovered by Reverdin[†] in the nitration of *p*-iodoanisole derivatives, the product from iodoanisole itself being 2-iodo-4-nitroanisole. Although iodine transfer to other nuclei has been observed, the good yield of iodonitroanisole suggests that iodine is not set free in the main reaction. The most reasonable mechanism seems to be:

[†] *Ber.* 1896, **29**, 1000.

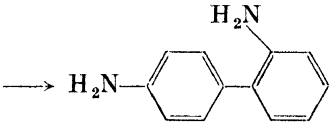


The benzidine rearrangement

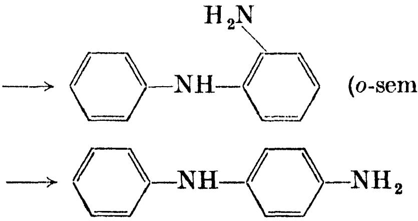
This reaction is treated separately since it presents special features. It has been investigated in greater detail than any of the others and it is of exceptional theoretical interest. Hydrazobenzenes can react in four different ways with acids. They can give benzidines



or diphenylines



or semidines



(*o*-semidine)

(*p*-semidine)

or they may disproportionate

$$2\text{Ph—NH—NH—Ph} \rightarrow \text{Ph—N{=}N—Ph} + 2\text{Ph—NH}_2.$$

The benzidine and semidine rearrangements are unimolecular,† and the former is almost certainly intramolecular since hydrazo-*o*-anisole and hydrazo-*o*-phenetole rearrange quite independently in admixture,‡ no methoxyethoxybenzidine being found in the products.

The effect of substituents on the proportions of the various products formed has been investigated in very great detail by Jacobsen and his collaborators.§ Dewar‖ has shown that the results can be expressed in a few simple generalizations. The first step in the reaction is formation of a salt with the acid catalyst; the proton will bind itself to the more basic nitrogen, and in unsymmetrical hydrobenzenes we may predict the relative basicities of the nitrogen atoms from the basic strengths of the corresponding aniline derivatives. Calling the more basic ring A, the less basic ring B, we may state the following rules, which suffice to explain the evidence available:

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† Biilman and Blom, *J.C.S.* 1924, **125**, 1719; Dewar, ibid. 1946, 777.

‡ Ingold and Kidd, *J.C.S.* 1933, 894.

§ Jacobsen, *Annalen*, 1922, **428**, 76.

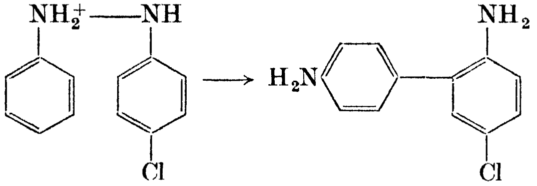
‖ *Nature*, 1945, **176**, 784.

1. Only the *para*-position in A can take part in diphenyline formation.
2. In semidine formation, ring A carries the $—NH_2$ in the product.
3. The ease of reaction falls in the series benzidine > diphenyline > semidine.
4. Disproportionation probably occurs in all cases to some extent, but is independent of rearrangement.

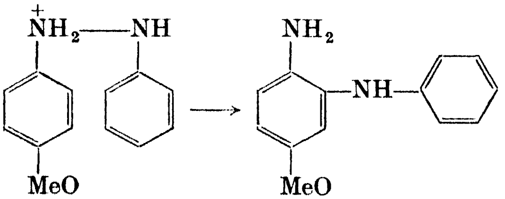
A few examples will illustrate the rules.

(*a*) Hydrazobenzene itself gives mainly benzidine with some diphenyline.

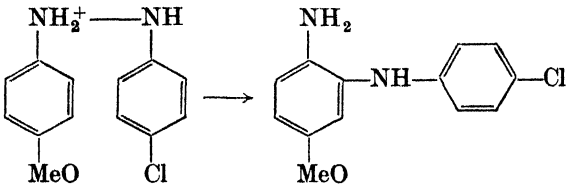
(*b*) *p*-Chlorohydrazobenzene cannot give a benzidine since one *para*-position is blocked. The unsubstituted ring is the more basic (A) so the main product is a diphenyline, the *para*-position in A being free.



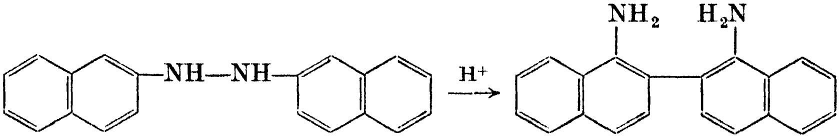
(*c*) *p*-Methoxyhydrazobenzene also is prevented from giving a benzidine. Moreover, the *para*-substituent is in the more basic ring and so diphenyline formation is also inhibited. The main product is a semidine.



(*d*) 4-Methoxy-4′-chlorohydrazobenzene also gives a semidine, in which the more basic (anisidine) ring carries the free amino group.



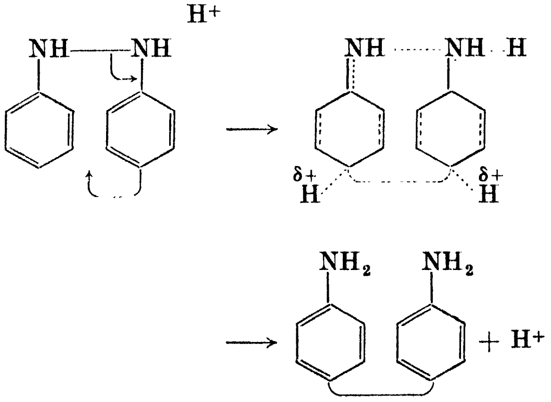
Slightly different rules apply in the hydrazonaphthalene series. Here diphenylines and *p*-semidines are never formed, but *o*-benzidines are. Thus β-hydrazonaphthalene gives 1:1′-diamino-2:2′-dinaphthyl with acid:



The order of preference is *p*-benzidine > *o*-benzidine > *o*-semidine. In the semidine the more basic ring again carries the free $—NH_2$. Examples will be found in Jacobsen's summary (see p. 233).

Mechanism of the benzidine rearrangement

Apart from earlier suggestions that benzidine is formed via semidines or other similar intermediates, four mechanisms for the reaction have been suggested. (It has been definitely proved that semidines are not intermediates since they do not rearrange to benzidines.) All these mechanisms recognize the analogy between the benzidine rearrangement, other rearrangements of N-substituted anilines, and normal aromatic substitution. Ingold and Kidd† and Hughes and Ingold‡ suggested that ionization of the N—N bond takes place, leaving two ions $PhNH^+$ and $PhNH^-$, of which the latter is then substituted normally in the nucleus by the cationoid $PhNH^+$. The whole reaction was thought to occur in one step, the *para*-positions combining simultaneously with the N—N fission, and the acid catalyst at the same time contributing a proton to the negative nitrogen. Thus:



Robinson§ suggested an alternative mechanism in which the proton first binds itself to the hydrazobenzene and the subsequent electron displacements then resemble those in the Ingold mechanism but in the reverse direction.

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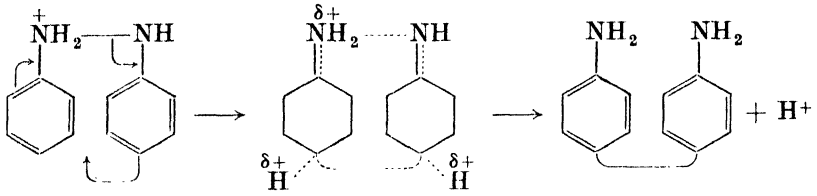
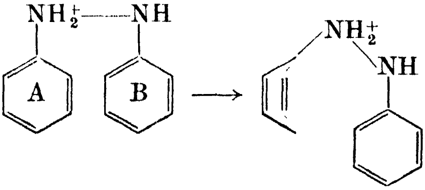
† *J.C.S.* 1933, 984. ‡ Ibid. 1941, 606. § Ibid. 1941, 220.



The Ingold mechanism seems unlikely since hydrazobenzene should have a basic *pK* of about 14 from analogy with aniline, diphenylamine, and phenylhydrazine, where each phenyl lowers the basic *pK* by *c.* 4 units. Salt formation of a base of that strength could hardly be a slow process. A further objection, which applies to both mechanisms, is the extraordinary configuration the molecule would have to adopt in the transition state. Even in molecular complexes aromatic rings do not approach closer than 3·7 A, and so in the transition states for the Ingold and Robinson mechanisms the N—N and *para*-C- -C bonds would be at least 3·7 A long. The bond-energy of bonds stretched to this extent is very small; therefore the transition state would have a small heat of formation, and the reaction would have a high activation energy and could only take place with difficulty.

Hammick and Mason† modified the Robinson mechanism by assuming that ring A in the hydrazobenzene could react in a buckled quinonoid form:



The *para*-position in such a 'boat' structure could approach the *ortho*- or *para*-position of ring B closely. This mechanism, though ingenious, is hardly satisfactory; it does not solve the equal stereochemical difficulties met in formulating rearrangements of other N-substituted anilines in classical terms, and, moreover, in producing such a transition state the whole resonance energy of one benzene ring (36 Cals.) would be lost, so that the activation energy of the reaction would be high.

The crux of the matter is that the two halves of the molecule must be held together somehow *after* the N—N bond has parted *until* the *para*-

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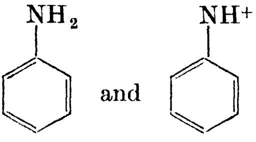
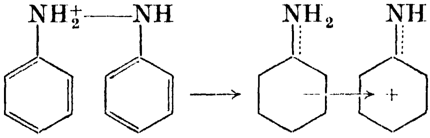
† *J.C.S.* 1946, 638.

carbon atoms (or two other points in the rings) can unite. Now ionization of the hydrazobenzene salt would give

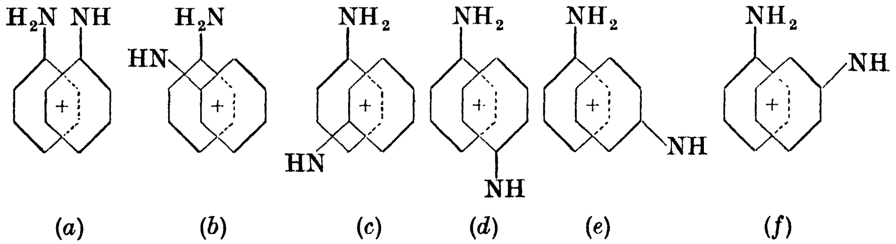


(A) (B)

of which (A) should be an excellent electron donor, the anionoid character of the π-electrons being increased by the −π amino group, while (B) will differ from it by having two electrons less, that is, the ion-radical Ph—NH⁺ will possess the same mesomeric structure as Ph—NH but will have one of its π-orbitals empty. Since the π-orbitals of (A) and (B) can overlap very efficiently, it should be possible for them to unite by forming a super molecular bond,† formed from a π-orbital of each component. Moreover, the conversion of the hydrazobenzene salt to this molecular complex can take place without any essential change in configuration, apart from a folding of the molecule to bring the rings together; hence the activation energy should be relatively low and at no time could the halves come apart:



The formation of the various reaction products from this π-complex can be explained very easily. Although the rings are symmetrical, the distribution of π-electrons round them will vary periodically, being most dense near the carbon nuclei. Therefore the six configurations (*a*–*f*) of the π-complex will be more stable than intermediate configurations. Moreover, conjugation with the nitrogen atoms further alters the electron density in the rings; the orientations (*a*, *c*, *e*) are therefore more stable than (*b*, *d*, *f*), since in the former the positions *o*–*p* to the nitrogen atoms are adjacent. And finally, the configuration (*a*) will be the most stable of all,



(*a*) (*b*) (*c*) (*d*) (*e*) (*f*)

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† Dewar, ibid. p. 406.

since in it the π-orbitals (which cover nitrogen as well as the rings) overlap most efficiently. The potential energy (E) of the molecule may then be represented somewhat as in Fig. 5.†

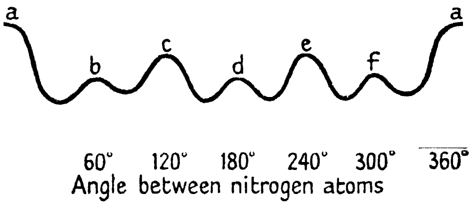
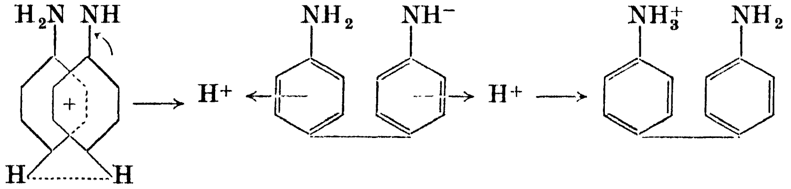


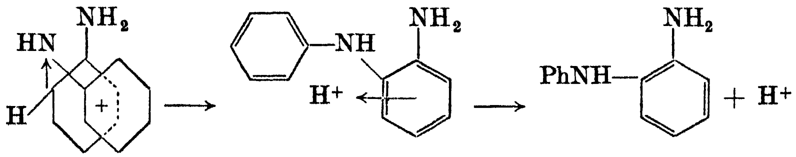
Fig. 5.

Any pair of opposite methine groups may combine in the π-complex, the molecular bond contracting into a σ-bond between the carbons, while the hydrogen atoms are displaced on to the π-electrons of the ring: e.g.



(Alternatively the hydrogens may be removed as H^+ by some other base.) Since this reaction is equivalent to the replacement stage undergonè by the π-complex in a normal substitution reaction, and since the most positive positions in ring B (the cationoid ring) will be those *o–p* to nitrogen, we should expect linkage to occur only between positions *o–p* to nitrogen in the rings; and also by analogy with the substitution reactions of aniline and the rearrangement reactions of N-bromacetanilide, etc., the *para*-position of ring A should react more readily than the *ortho*. If we also remember that the most stable form of the π-complex, and the one formed initially, is (a), it is easy to understand why benzidine is formed in preference to diphenyline, why only the *para*-position of ring A takes part in diphenyline formation, and why *o*-benzidines are not formed.

Since the positive charge in ring B is shared by the nitrogen atom, an alternative reaction is possible, leading to a semidine, the nitrogen linking with an *o*- or *p*-carbon in the other ring.



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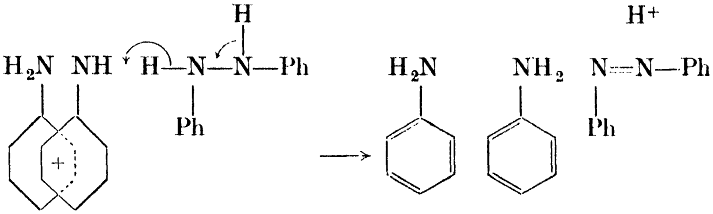
† These conclusions are in accord with the results of quantum-mechanical calculation; see Dewar, *Faraday Society Discussion on the Labile Molecule*, 1947.

Since the configuration leading to *o*- and *p*-semidines (*b*, *c*, *e*) are energetically unfavourable, semidines are formed less readily than benzidines or diphenylines.

In this way the various empirical rules governing the course of the reaction can be explained. The disproportionation may be ascribed to a cationoid removal of H^- from hydrazobenzene by the π-complex:



It is interesting that hydrazobenzene forms coloured salts in aprotic solvents,† the colour differing from that of the parent base or of its rearrangement products; on adding water, little hydrazobenzene is regenerated, the main products being benzidine and diphenyline (whose salts are colourless). It seems very likely that the 'salt' of hydrazobenzene really contains our π-complex as the cation, in equilibrium between its various configurations. The further reaction is inhibited by lack of a proton acceptor; on adding water the various isomeric forms of the complex give corresponding rearrangement products. The colour parallels that of solutions of aromatic hydrocarbons in anhydrous HF (p. 169).

Hydrazonaphthalene should give an analogous π-complex, but in it rotation of the components will only be possible at the expense of a great decrease in overlapping of the π-orbitals forming the molecular bond (which cover both rings). Therefore such rotation will be very unfavourable, and hence diphenylines and *p*-semidines are not formed. But since the *o*–*p* positions in α-naphthylamine differ less in reactivity than those in aniline, and since in β-naphthylamine the adjacent α-position is strongly activated for cationoid substitution, both α- and β-hydrazonaphthalene can give *o*-benzidines.

Recently kinetic evidence has been found for the π-complex mechanism.‡ Salt-formation definitely seems to precede rearrangement, in disagreement with the Ingold mechanism. Also the observed activation energies (12–19 Cals.) are too low for the Hammick–Mason mechanism to be possible. And finally, the measurements provide an argument against the Robinson mechanism. This requires the N—N bond to break in such a way that electrons recede from a positive centre; therefore appreciable bonding of the *para*-carbons would have to precede any extensive weakening of the N—N bond. In that case the rate of reaction should depend on the ease of cationoid attack by the *para*-position of ring A on that of ring B. Since methoxyl will not greatly affect the cationoid reactivity of ring A, but will greatly increase the anionoid reactivity of a position *ortho* to it in ring B and decrease that of a *meta*-position (since its action is +I, −E), the Robinson mechanism would require the ions (I), (II), and (III) to rearrange in the order of rates (I) $\gg$ (II) $>$ (III).

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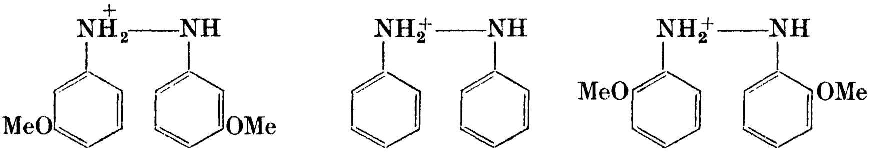
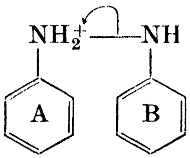
† Orelkin, Rysskaltschuk, and Aisikowitsch, *J. Gen. Chem. U.S.S.R.* 1931, **1**, 696.

‡ Dewar, *J.C.S.* 1946, 777.



(I) (II) (III)

According to the π-complex mechanism the first step is a conversion of the N—N bond into a molecular bond. This will be accelerated by substituents which increase the polar character of the N—N bond in the salt and so weaken it. The electron displacement



will be facilitated by an *o*-MeO in ring B, retarded by *m*-MeO, but it will be little affected by methoxyl in the other ring where the E-effect of the substituent is not called into play. Therefore we should expect the ease of rearrangement of the three ions to be (I) $<$ (II) $\ll$ (III), that is, exactly the reverse of that predicted by the Robinson mechanism. The order of rates observed agreed with that predicted by the π-complex theory.

The methoxy group is a particularly valuable weapon in studying aromatic reactions because as a substituent it has opposed, and quite strong, I- and E-effects (cf. p. 173).

CHAPTER XII

RADICALS OF LONG LIFE

In the reactions so far considered, bonds are formed or broken by the transfer of electrons in pairs with opposite spins. The reactions are essentially ionic, for when a bond breaks in this way, one of the atoms forming it acquires a positive, the other a negative charge. It has long been known that in hexaarylethanes an alternative mode of fission is possible, the bond between the central carbons breaking symmetrically so that each of the two carbon atoms acquires one of the bonding electrons. The products are molecules with odd numbers of electrons, that is, they are radicals. The odd electron in a radical is best represented by a dot, thus:

$$Ph_3C—CPh_3 \rightleftharpoons 2Ph_3C\cdot$$

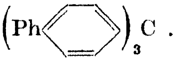
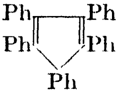
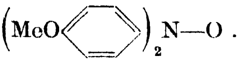
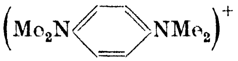
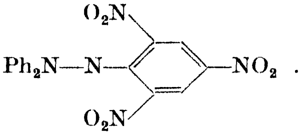
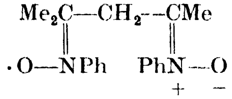
The original evidence for the fission of hexaphenylethane to triphenylmethyl radicals was the extraordinary ease with which the parent hydrocarbon gave products in which the central bond was broken; thus with oxygen it forms triphenylmethyl peroxide,

$$Ph_3C—CPh_3 \rightarrow 2Ph_3C\cdot \xrightarrow{O_2} Ph_3C—O—O—CPh_3$$

and with halogen, triphenylmethyl halides. Moreover, solutions of hexaphenylethane are coloured, unlike the crystalline solid, and the colour deepens with increasing temperature, as would be expected if it were due to reversible dissociation. Moreover, other hexaarylethanes were soon found to be dissociated even more readily than hexaphenylethane, and the dissociation could then be established and measured by molecular weight determination.

Final proof that dissociation of C_2Ph_6 gives free radicals came, however, from magnetic measurements; solutions of the hydrocarbon are paramagnetic (cf. p. 40). Indeed magnetic measurements provide the most reliable method for measuring the degree of dissociation of hexaphenylethane derivatives. The situation is somewhat complicated by the fact that the observed susceptibility depends both on the degree of dissociation of the hydrocarbon into radicals, and on the magnetic susceptibility of the latter. However, since the susceptibility of radicals is almost entirely due to the spin of the odd electron, the susceptibilities of radicals are similar and approximately equal to the theoretical value (1270×10^{-6}) for a free electron. Some examples of monomeric radicals are given in Table 27. Thus if the observed paramagnetic susceptibility of a compound is $x \times 10^{-6}$, the degree of dissociation into radicals will be approximately $x/2540$; because complete dissociation would give two radicals each with a susceptibility of approximately 1270×10^{-6}.

TABLE 27

Compound	$x_p \times 10^6$
	1,200
	1,200
	1,200
	1,250
	1,120
 $\begin{array}{ccc}\mathrm{Me_2C} & \mathrm{—CH_2—} & \mathrm{CMe} \\ \| & & \| \\ \cdot\mathrm{O—NPh} & & \underset{+}{\mathrm{PhN}}—\underset{-}{\mathrm{O}}\end{array}$	1,290
$(\mathrm{KSO_3})_2\mathrm{N—O}\cdot$	1,140
$(\mathrm{AgPy_4})^{++}\mathrm{S_2O_8^{--}}$	1,040
NO	1,475
$\mathrm{NO_2}$	1,410
$\mathrm{ClO_2}$	1,370

Kenyon and Sugden, *J.C.S.* 1932, 170; Allen and Sugden, ibid. 1936, 440; Sugden, *Trans. Faraday Soc.* 1934, **30**, 18; Müller, Müller-Rodloff, and Bunge, *Annalen*, 1935, **520**, 235; *Ber.* 1936, B **69**, 665; Michaelis and Granick, *J.A.C.S.* 1943, **65**, 1747.

Nature of stable free radicals

According to our definition of bond-energies, the energy required to break a C—C bond in a compound to give two radicals should be equal to the C—C bond-energy, i.e. 81 Cals. The energy required to break the C—C bond in hexaphenylethane may be estimated from the equilibrium between it and triphenylmethyl; it amounts to 9·9 Cals.† Therefore either the C—C bond in hexaphenylethane must be weakened to the extent of 71 Cals., or the radicals formed by its fission must be stabilized by mesomerism. The weakening of the bond can be estimated from measurement of heats of reactions where it is broken; the heat of hydrogenation of hexaphenylethane to two moles of triphenylmethane indicates that the bond is 27 Cals. weaker than that in ethane, while the heat of oxidation leads to the value 35 Cals.‡ Therefore only part of the anomalous ease of dissociation can be ascribed to bond-weakening. (We may add that the 'weakening' of the bond is probably purely mechanical in origin, representing the strain in the molecule due to the close packing of the bulky aryl groups. The central bond in hexamethylethane is also longer and weaker than that in ethane).

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† Preckel and Selwood, *J.A.C.S.* 1941, **63**, 3397.

‡ Bent and Cuthbertson, ibid. 1936, **58**, 170.

The triphenylmethyl anion is mesomeric (p. 11), the eighteen π-electrons of the ring-carbons, and the two unshared p-electrons of the central carbon occupying extended orbitals covering all nineteen carbon atoms. The orbitals differ considerably in energy, and the electrons in the highest orbital will contribute little to the total binding-energy of the molecule. Therefore removal of one of these electrons should leave a radical with almost the same resonance energy as the parent anion. It is interesting that the resonance energy of the triphenylmethyl radical calculated from the thermochemical measurements referred to above (25 Cals.) is of the same order as that calculated for the triphenylmethyl anion from the difference in acid pK between triphenylmethane and paraffins.

From this general argument it is clear that a radical will be stabilized if it is derived from a mesomeric anion by loss of one electron. Therefore a radical will be stabilized by adjacent +E substituents, and less strongly by adjacent +I substituents. An alternative mode of stabilization, by negative substituents, is also possible. Consider a radical with an adjacent −E substituent:

$$\mathrm{X{—}C}\cdot$$

Removal of the odd electron would leave a mesomeric cation:

$$\mathrm{X{—}C}\cdot \rightarrow \overbrace{\mathrm{X}\overset{\cdots}{\text{—}}\mathrm{C}}^{+} + \textcircled{e}$$

Although all the bonding orbitals in the cation will be full, the extra heat of formation due to the extra bond in it may be such that addition of the odd electron to an antibonding orbital (p. 8) may give a system of stability comparable to that of the original non-mesomeric radical. In that case the actual state of the radical will be mesomeric between the two structures and it will therefore be more stable than either,

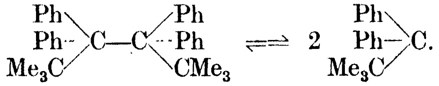
$$\mathrm{X{—}C}\cdot \longleftrightarrow \mathrm{X}\overset{\cdots}{=}\mathrm{C}$$

the dotted line in the latter formula representing the one-electron 'antibond'. Thus radicals should be stabilized by all substituents. In practice the stabilization due to E-substituents is much greater than that due to I-substituents, and by +E greater than by −E.

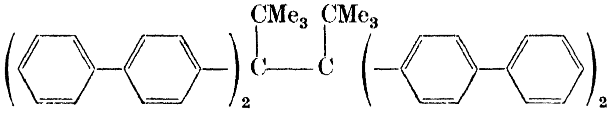
Since benzyl and benzhydryl radicals should also be mesomeric, we might expect the central bonds in dibenzyl and in tetraphenylethane to be likewise weakened. Actual dissociation into radicals can be demonstrated in dimethyl-, diethyl-, and dipropyl-tetraphenylethanes from their reactions with oxygen to form alkyl-diphenylmethyl peroxides:

$$\mathrm{Ph_2CR{—}CRPh_2} \rightarrow \mathrm{2Ph_2CR}\cdot \xrightarrow{\mathrm{O_2}} \mathrm{Ph_2CR{—}O{—}O{—}CRPh_2}.$$

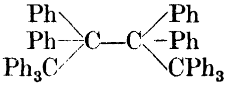
From the rate of reaction at different temperatures it is possible to find the activation energy of this reaction which must set an upper limit to the energy required to break the parent ethane into radicals. The value found† was 27 Cals. Evidently the same effect operates again but to a smaller extent, partly because the resonance energy of the benzhydryl radical is less than that of the triphenylmethyl radical, but probably mainly because the steric hindrance between the phenyls is smaller when there are only four of them in the molecule, so that the central bond in the ethane is less weakened. This is made likely by the observation‡ that *bis*(*tert*-butyl)tetraphenylethane dissociates measurably into radicals in solution, the steric hindrance being once more increased by the presence of the bulky *tert*-butyl groups:



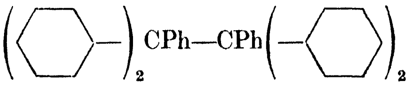
The same effect is observed§ in the analogous compounds



and



and peroxide formation is observed|| even in



a dibenzyl derivative.

Structure and stability

From the above discussion it will be clear that both steric and electronic factors are of importance in determining the readiness with which hexaarylethanes dissociate. We should expect substituents which increase the ±E effect of phenyl to increase dissociation; and indeed the *p*-biphenylyl, *p*-tolyl, and *p*-nitrophenyl groups are more efficient than phenyl itself (Table 28). But we should also expect dissociation to be increased by bulky substituents which increase the steric strain in the parent ethane; and clearly the activity of *m*-biphenylyl, and the extraordinary activity of *o*-tolyl, can be explained in no other way. The *o*-methyl groups will be particularly effective in increasing the strain. Nevertheless, the complete dissociation of hexa(*o*-tolyl)ethane is most remarkable since the *o*-methyls must also greatly reduce the mesomerism of the corresponding radicals by steric hindrance of a planar configuration (cf. p. 205).

The dissociation of hexaarylethanes cannot therefore be related to their

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† Ziegler, Seib, Knoevenagel, Herte, and Andreas, *Annalen*, 1942, **551**, 150.

‡ Conant and Bigelow, *J.A.C.S.* 1928, **50**, 2041.

§ Conant and Schultz, ibid. 1933, **55**, 2098; Schlenk and Mark, *Ber.* 1922, **55**, 2285.

|| Ziegler, *Annalen*, 1942, **551**, 127.

structure in terms of electronic theory only. This point is still further emphasized by the large and variable entropies of dissociation that have been observed (Table 29). The assumptions that entropy changes are constant, and that bond-energies are effected only by mesomerism and induction, here break down completely.

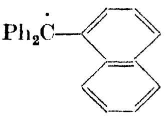
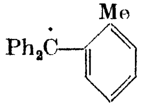
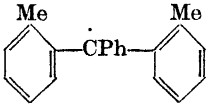
TABLE 28

Per cent. dissociation of 0·1 *M solution in benzene at* 25°

X	$(Ph_2CX)_2$	$(PhCX_2)_2$	$(CX_3)_2$
Ph	—	—	2·8
p-Tolyl	5	5·5	16
m-Tolyl	6·5	7·0	40
o-Tolyl	25	82	100
o-Ethylphenyl	33	—	—
p-(*n*-Propyl)phenyl . . .	6·5	—	21
p-*iso*Propylphenyl . . .	9	8	26
p-*tert*Butylphenyl . . .	7·5	8·5	43
o-Anisyl	3·8	7·3	42
p-Anisyl	4·4	—	—
p-Nitrophenyl	—	—	63
p-Fluorophenyl	—	—	5·2
p-Biphenylyl	11	18	26
m-Biphenylyl	12	—	40
α-Naphthyl	25·2	—	—
β-Naphthyl	6	13	24 (0·0125 M)

Marvel, Ginsberg, and Mueller, *J.A.C.S.* 1939, **61**, 77; Marvel, Mueller, and Ginsberg, ibid., p. 2008; Marvel, Kaplan, and Himel, ibid. 1941, **63**, 1892; Marvel, Whitson, and Johnson, ibid. 1944, **66**, 415; Marvel, Dietz, and Himel, *J. Org. Chem.* 1942, **7**, 392; Allen and Sugden, *J.C.S.* 1936, 440; Theilacker and Ewald, *Naturwiss.* 1943, **31**, 302; Preckel and Selwood, *J.A.C.S.* 1941, **63**, 3397.

TABLE 29

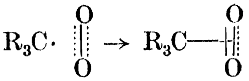
Radical	*% dissociation,* 0·03 *M sol. at* 20°	ΔF (Cals.)	ΔH (Cals.)	ΔS (cals./°C.)
$Ph_3C\cdot$	2·8	5·2	9·9	16
	25·2	2·7	11·5	30
	19·7	2·6	11·4	29
	90·8	0·7	8·6	27

Preckel and Selwood, *J.A.C.S.* 1941, **63**, 3397.

Oxygen and nitric oxide

A radical contains at least one orbital with an unpaired odd electron; therefore two radicals can in general combine directly with one another, using their odd orbitals and two odd electrons to form a σ-bond. Such reactions of non-mesomeric radicals will be highly exothermic and so radicals have long lives only if they are stabilized by mesomerism, their tendency to dimerize being thus decreased.

Carbon radicals also have a very high affinity for oxygen, as we have already remarked. Now oxygen (p. 18) contains two unpaired electrons occupying separate π-orbitals with parallel spin; these π-orbitals can be used for bond-formation with other radicals, the bonds being molecular bonds, e.g.



$$R_3C\cdot\ \overset{O}{\underset{O}{\vdots\|\vdots}} \rightarrow R_3C-\overset{O}{\underset{O}{\|}}$$

One might have expected oxygen to dimerize to O_4 by a similar mechanism. However, the triplet state of O_2 is more stable than the singlet (p. 18) because in it the two unpaired electrons have parallel spins; and this spin-interaction energy would be lost in forming a normal molecule (O_4) in which all the electrons were paired. The same effect accounts for the failure of nitrogen, oxygen, and sulphur radicals to combine with oxygen, the spin-interaction energy of O_2 being comparable with the O—O, N—O, and S—O bond-energies. Carbon radicals do react, the C—O bond-energy being much larger.

Nitric oxide is itself a stable radical; it has the same electronic structure as oxygen, but contains one extra electron. One of the outer π-orbitals of oxygen now contains an electron-pair. However, nitric oxide can resonate between the forms with its odd electron in either of the outer orbitals and so is stabilized. It has therefore little tendency to dimerize or combine with mesomeric carbon radicals. It does, however, combine readily with non-mesomeric radicals such as methyl or ethyl and also with nitrogen radicals such as Ph_2N (forming nitrosamines). In the latter case the product is also mesomeric, and so reaction is facilitated.

$$Ph_2N\cdot + N\overset{\cdot\,\cdot\,\cdot}{\equiv}O \rightarrow Ph_2\overset{\delta+}{N}\overset{\cdots}{=}N\overset{\cdots}{=}\overset{\delta-}{O}$$

Hetero-radicals

Since the bonds O—O, N—N, and S—S are much weaker than C—C, compounds containing the former should dissociate much more readily into radicals than do hydrocarbons, and of course the fission will be facilitated by substitution in a similar way. Many examples are known; thus tetraphenylhydrazine dissociates reversibly to diphenylnitrogen radicals† (I), and similar oxygen and sulphur radicals are known (e.g.

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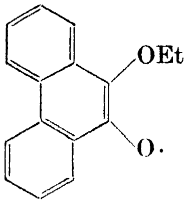
† Wieland, *Annalen*, 1911, **381**, 212; 1912, **392**, 156.

(II),† (III)‡). Moreover, tritolylamine with bromine gives salts containing the ion-radical§ (IV), which bears the same relation to (I) that ammonium ions do to amines.

$Ph_2N\cdot$

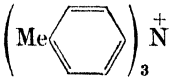
(I)



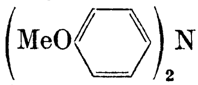
(II)

$Ph—S\cdot$

(III)



(IV)

If hexaphenylethane is allowed to react with tetraanisylhydrazine, the $Ph_3C\cdot$ and  N · radicals formed by dissociation combine to the stable $Ph_3C—N(anisyl)_2$ which does not dissociate measurably at normal temperatures. This is an amusing illustration of a general rule that the heat of formation of a bond X—Y between dissimilar elements X, Y is more than the mean of the heats of formation of X—X and Y—Y. Hence the reaction

$$Ph_3C\cdot CPh_3 + Ph_2N\cdot NPh_2 \rightarrow 2Ph_3C\cdot NPh_2$$

should be exothermic and the heat of dissociation into radicals of the product greater than those of the reactants.

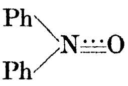
Another very interesting type of radical (VI) was reported by Wieland and Offenbacher,‖ being obtained by oxidation of diphenylhydroxylamine (V). The radical is stabilized by the adjacent —E nitrogen and probably approximates to the structure (VII) where the odd electron occupies an antibonding π-orbital, its high energy being compensated by formation of a normal π-bond between N and O, which, moreover, can conjugate with both phenyls.

$Ph_2N—OH$

(V)

$Ph_2N—O\cdot$

(VI)



$$\begin{matrix} Ph \\ & \rangle N \overset{\cdot\cdot}{=} O \\ Ph \end{matrix}$$

(VII)

The hydrazyl radicals discovered by Goldschmidt†† are of similar type, the oxygen being replaced by NX where X is a +E group. We should expect the stability of the radical $R_2N—NX$ to be increased by increasing the negativity of R or the positivity of X. In the three series of compounds (VIII), (IX), and (X) Goldschmidt found that the radical stability varied with R, the stability rising in the series

$$R = NO_2 < Br < H < Me < MeO < Me_2N;$$

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† Goldschmidt, Vogt, and Bredig, ibid. 1925, **445**, 123.

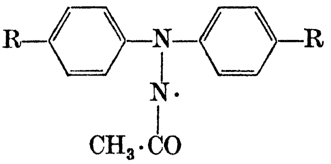
‡ Schönberg and Rupp, *Naturwiss.* 1933, **21**, 561.

§ Weitz and Schwechten, *Ber.* 1926, **59**, 2307.

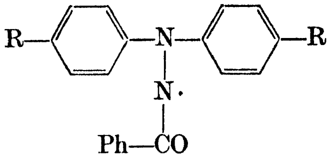
‖ Ibid. 1914, **47**, 2111.

†† Ibid. 1920, **53**, 44.

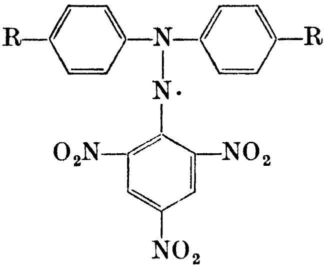
while for a given R stability increased in the order (VIII) < (IX) < (X). These results are in accord with our predictions.



(VIII)



(IX)

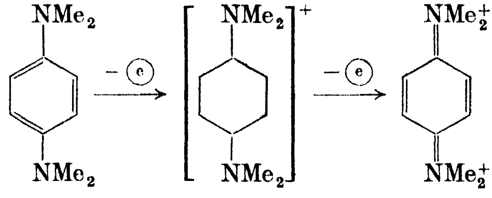


(X)

The radical (X) with R = Me_2N is particularly interesting, being so stable that no sign of dimerization can be detected.

Würster salts

The oxidation of *p*-phenylenediamine derivatives to salts of quinonediimines has long been known to occur via highly coloured intermediates, the so-called Würster salts.[†] Thus complete oxidation of tetramethyl-*p*-phenylenediamine (XI) gives the weakly coloured diimine salt (XIII), by removal of two electrons; but a highly coloured intermediate can be isolated containing the monomeric cation (XII).



(XI) (XII) (XIII)

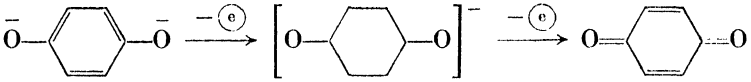
The structure of the Würster salts has been established by Michaelis and his collaborators.[†] It is evident from their mode of formation that their cations contain odd electrons and are therefore radicals. Michaelis found that their solutions were indeed paramagnetic. The electronic structure of such an ion-radical presents no special problem since it is derived from the parent mesomeric diamine by loss of one electron, just as is triphenylmethyl from the Ph_3C^- ion. It is interesting that the molecular orbital of highest energy in *p*-phenylene diamine is localized on the four central carbon atoms of the ring, so in the Würster salt the electron deficiency will also be localized there.

[†] For reviews see Michaelis, *Chem. Rev.* 1935, **16**, 243; Michaelis and Schubert, ibid. 1938, **22**, 437. Also numerous papers in the *J.A.C.S.*

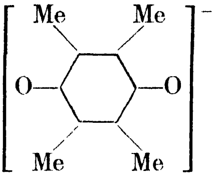
Quinhydrones

Hydroquinone and quinone combine to form a highly coloured solid, quinhydrone, which dissociates into its components in solution. Its structure is still uncertain and at present the most reasonable view seems to be that in the crystal the components are held together by some kind of π-electron sharing, quinone behaving as an electron acceptor since it is derived from the aromatic dianion of hydroquinone by loss of two electrons.

Now hydroquinone in alkali might give a Würster salt intermediate by loss of one electron:



it can be shown polarographically (*vide infra*) that such an intermediate is actually formed in the alkaline oxidation of hydroquinone, but it cannot be isolated. The more stable ion-radical



from durohydroquinone seems, however, to form definite salts. There is therefore some connexion between Würster salts and quinhydrones.

If a quinhydrone is formed by π-electron interaction from its parent quinone and hydroquinone, the former acting as electron acceptor, the latter as donor, a similar compound should be formed from a Würster salt by direct combination of radicals. Now such combination will involve fusion of the individual one-electron orbitals into extended orbitals of some kind, which the odd electrons will naturally occupy in pairs with opposite spins. Formation of a quinhydrone by polymerization of a Würster salt should then lead to a pairing of the spins of the odd electrons, the quinhydrone being diamagnetic. Michaelis actually finds that Würster salts from *p*-phenylenediamines can be divided sharply into two categories.† The first, containing no hydrogen attached to nitrogen, are paramagnetic in the solid state as well as in solution, and the actual value of the magnetic susceptibility indicates that no polymerization of the radicals takes place. The second, where the terminal nitrogen atoms carry hydrogen, are paramagnetic in solution but diamagnetic in the solid state. These must then form quinhydrones, and hence it seems likely that the electron sharing by which quinhydrones are formed involves some kind of hydrogen bond, although the details are still obscure.

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† Michaelis and Granick, *J.A.C.S.* **1943, 65, 1747.**

Oxidation-reduction ; the polarograph

If an inert electrode is placed in a solution of two substances X, X^- differing only by one electron, it acquires a definite potential depending only on the relative concentrations of the solutes; the potential being such that the tendency of X to acquire electrons from the electrode is equal to the tendency of X^- to give electrons to it. The potential thus provides a measure of the oxidizing (electron-accepting) power of X, or the reducing (electron-donating) power of X^-. The potential measured relative to the hydrogen electrode under standard conditions (the concentrations of X and X^- being equal) is called the redox potential of X. The higher the potential, the stronger X is as an oxidizing agent.

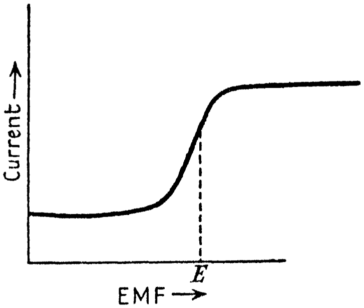


Fig. 6.

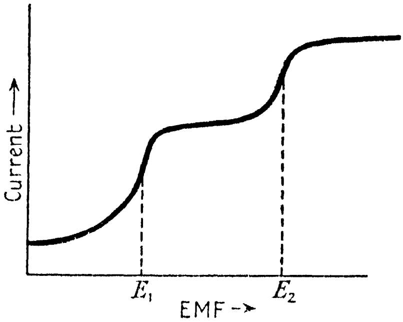
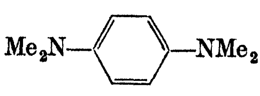


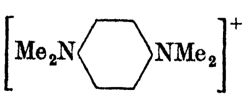
Fig. 7.

The polarograph uses a special modification of this principle. In it a variable potential is applied between two electrodes in the solution, one formed by a pool of mercury, the other by mercury dropping from a capillary so that its effective surface is continually being reformed. When the potential between the electrodes exceeds a value depending on the redox potential of the solute, the current flowing between them increases suddenly. In the polarograph the current is plotted automatically against the applied potential, and hence a 'wave' is obtained, marking the critical potential from which the redox potential (E) of the solute may be found (Fig. 6).

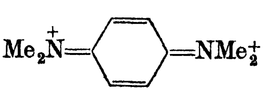
Now if a solution of tetramethyl-*p*-phenylenediamine (XIV) is examined in this way it is found to give two waves (Fig. 7); one (E_1) corresponding to oxidation of (XIV) to the Würster salt (XV), and the other (E_2) to the oxidation of (XV) to (XVI); because (XV) has an intermediate state



(XIV)



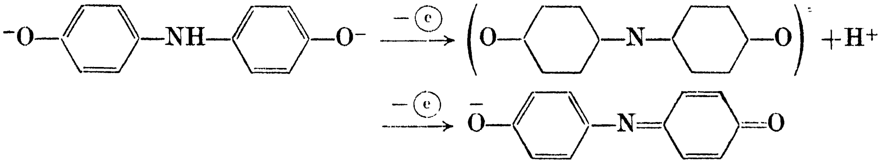
(XV)

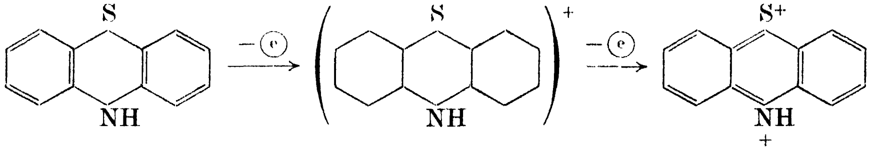


(XVI)

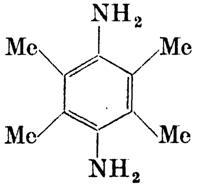
of oxidation between (XIV) and (XVI), and so its redox potential must differ from that of (XIV). Conversely, the appearance of two waves in a polarograph indicates the formation of an intermediate oxidation product. The polarograph is therefore most useful in the study of Würster salts, since by it the transient formation of ion-radicals can be established when isolation of them is impossible.

In this way Michaelis has demonstrated that the majority of oxidations where a product is formed by loss of two electrons take place via definite ion-radical intermediates; indophenol in alkali and thiodiphenylamine in acid are good examples:

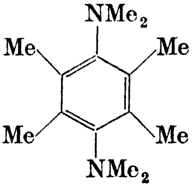




He has also established two further points. First, the stability of a Würster salt depends on the mesomerism of the related anion. If this mesomerism is sterically inhibited, no Würster salt is formed. Thus tetramethyl-*p*-phenylenediamine and diaminodurene (XVII) give stable Würster salts, but tetramethyldiaminodurene (XVIII) does not even give a second wave in the polarograph. The small NH_2 group is known to conjugate with the ring in durene, unlike the larger NMe_2 (p. 201).

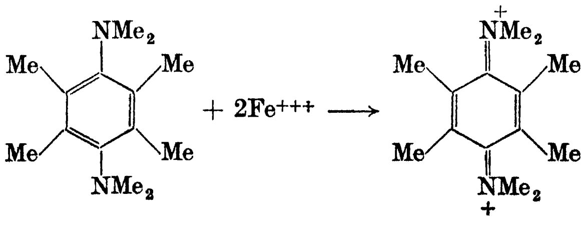


(XVII)

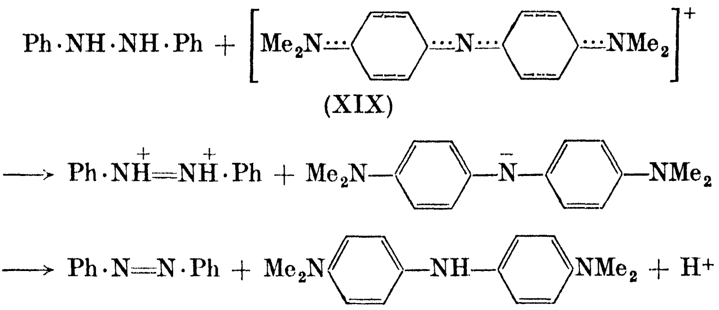


(XVIII)

Secondly, in cases where no Würster salt intermediate can be formed, oxidation is possible only by the simultaneous removal of two electrons. Thus oxidation of (XVIII) by ferric ion would require a termolecular reaction, and this does not occur at an appreciable rate.

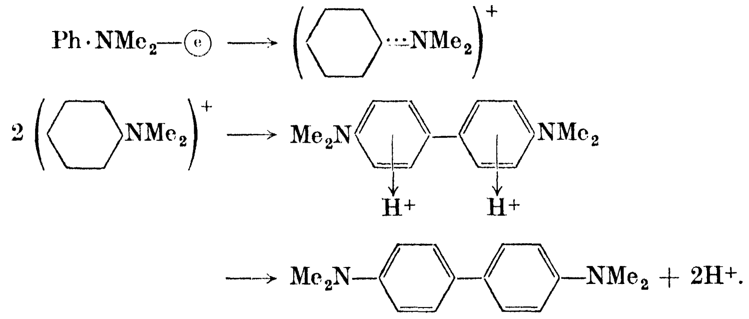


A very striking example is the instantaneous oxidation of hydrazobenzene to azobenzene by Bindschedler's green (XIX), a redox indicator, which can


(XIX)

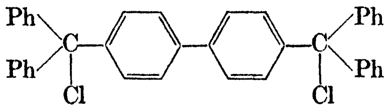
take up two electrons at once; in contrast to its non-oxidation by ferric chloride even on boiling. Ferric chloride is a more powerful oxidant than Bindschedler's green, but can only accept single electrons; and apparently the ion-radical from hydrazobenzene is too unstable to be formed as an oxidation intermediate.

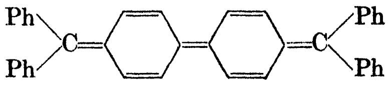
It is interesting that phenols and anilines give double waves in the polarograph, and their oxidative dimerizations probably take place through Würster salt intermediates; e.g.

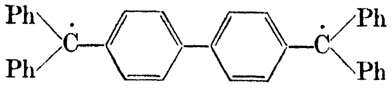


Diradicals

Treatment of the dichloride (XX) with 'molecular silver' gives a diamagnetic product which is best represented as the quinone (XXI). If the substance were the diradical (XXII), with a σ-bond between the central rings about which free rotation was possible, the spins of the two odd electrons would be independent; statistically half the molecules of (XXII) at any time would be diamagnetic, half paramagnetic with twice the magnetic susceptibility of triphenylmethyl, and so on average (XXII) would be paramagnetic with about the same moment as triphenylmethyl.

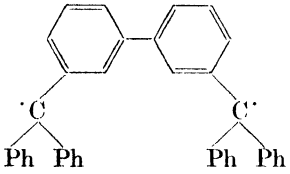

(XX)


(XXI)

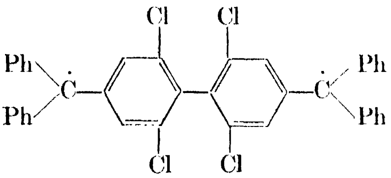


(XXII)

On the other hand, (XXIII) is paramagnetic and apparently does exist as a true diradical in solution. Here a quinonoid structure is not possible. The same, moreover, is true of the diradical (XXIV) where the coplanar configuration of the central rings, necessary for the quinonoid structure to be formed, is sterically hindered. It is interesting that asymmetric derivatives of 2:2′:2″:2‴-tetrachlorodiphenyl can be resolved, proving that a coplanar arrangement of the rings is indeed hindered.



(XXIII)



(XXIV)

Although (XXI) is diamagnetic, it is coloured in solution and can catalyse the interconversion of *ortho*- and *para*-hydrogen,† a property confined to highly magnetic substances. One possible explanation may be that the isomeric structures (XX) and (XXI) differ little in energy, the former being the more stable. As long as the central rings are coplanar, the structure will be quinonoid, but since (XXI) and (XXII) differ little in energy, rotation about the central bond will be quite easy, and in the intermediate states the molecule will be essentially a diradical. However, since the diradical is by hypothesis less stable than the quinone, it will exist only transitorily, and since reversing the spin of an electron is a relatively difficult process, and since the odd electrons have antiparallel spins in the quinone, the majority of molecules in the diradical state will also have their odd-electron spins paired and will therefore be diamagnetic.

A second way in which a normal diamagnetic mesomeric molecule may assume the properties of a diradical is by electronic excitation. In the normal molecule the π-electrons fit in pairs into the orbitals of lowest energy available. Now if the lowest unoccupied orbital differs little in energy from the highest occupied orbital, it may be quite easy for one of the electrons in the latter to pass into the higher orbital; and since the molecule now contains two odd electrons in separate orbitals, in its most stable state the odd electrons will have parallel spins (cf. p. 11). Hence the 'excited' (triplet) form of the molecule will be essentially a diradical, having, like O_2, two unpaired electrons, and, again like O_2, it will be paramagnetic. The best illustration of this phenomenon seems to be porphyrindine (XXV), which in the form written has no unpaired electrons and should be diamagnetic. Actually solutions of porphyrindine are paramagnetic,† and the magnetic susceptibility increases with temperature, indicating equilibrium with a less stable paramagnetic form. This 'triplet' state may be written formally as (XXVI), although it is of course actually mesomeric. Similar singlet-triplet equilibria may account for the properties of pentacene (XXVII) and other similar polycyclic hydrocarbons, which show many of the reactions of free radicals, and for the thermochromic behaviour of (XXVIII)‡ and (XXIX).§

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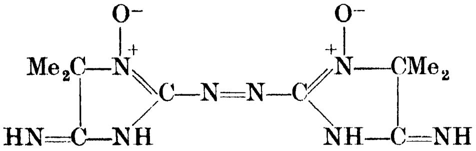
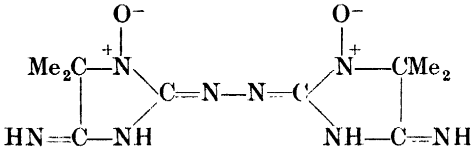
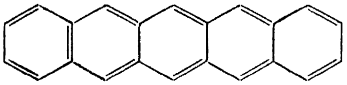
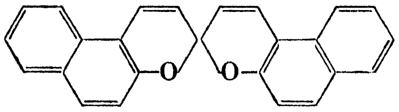
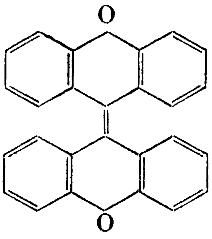
† Schwab and Agliardi, *Ber.* 1940, **73**, 95.


(XXV)


(XXVI)


(XXVII)


(XXVIII)


(XXIX)

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† Müller and Müller-Rodloff, *Annalen*, 1936, **521**, 81.
‡ Dilthey and Wizinger, *Ber.* 1926, **59**, 1856.
§ Schönberg, Ismail, and Asker, *J.C.S.* 1946, 442.

CHAPTER XIII

REACTIONS INVOLVING RADICAL INTERMEDIATES

It has been known for some time that simple aliphatic radicals, such as methyl, can be prepared in the gas phase by a variety of methods, and are stable, although their chemical reactivity is so great that they have only a momentary existence. Such radicals do not differ in kind from the stable triarylmethyl radicals discussed in the last chapter. They are far more reactive, not being stabilized by mesomerism, and radicals of all intermediate degrees of stability may be prepared. In recent years it has been shown that such highly reactive radicals are transient intermediates in many reactions.

Radicals may be prepared by three general methods. Firstly, by thermal decomposition of molecules containing weak bonds. The molecule splits into two radicals by fission at the point of weakness. This method is of course entirely analogous to the preparation of triphenylmethyl from hexaphenylethane; in the latter case the central C—C bond is effectively weakened by steric strain and by mesomeric stabilization of the resulting radicals. The metal-carbon bonds in metal alkyls are particularly weak, and pyrolysis of such compounds (e.g. $PbMe_4$) has been used to prepare alkyl radicals in the gas phase. In ordinary organic chemistry the most usual sources of radicals have been peroxides containing the weak O—O bond, or compounds such as diazotates which can eliminate molecular nitrogen with the formation of radicals, the driving force being the extremely high heat of formation of the N_2 molecule; e.g.

$$\mathrm{Ph\cdot N{=}N\cdot OH \rightarrow Ph\cdot + N_2 + \cdot OH}$$

A second method resembles the first in that radicals are formed by fission of one bond in the molecule, but the energy required for this fission is supplied in the form of light. Absorption of one quantum of light of λ 3,000 A by a molecule is equivalent to absorption of 100 Cals./Mol., so that the energy of ultra-violet light is sufficient to rupture bonds. A good example is the photolysis of acetone in the vapour phase to methyl and acetyl radicals. In inert solution, no reaction occurs because the nascent radicals are surrounded by solvent and so cannot easily diffuse apart; as a rule they therefore recombine (the so-called *primary recombination* effect, first pointed out by Franck and Rabinowitsch†). If substances which can easily react with radicals are present in the solution, however, the radicals may react rather than recombine. The main application of photochemistry in organic reactions has been the production of halogen atoms by photolysis of halogens; the atoms being used to initiate radical chains (*vide infra*).

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† *Trans. Faraday Soc.* 1934, **30**, 120.

The third method for preparing radicals consists in adding one electron to, or removing one electron from, a normal molecule, reactions exactly analogous to the production of a Würster salt either by reducing the corresponding quinone or oxidizing the corresponding hydroquinone. A simple illustration is the preparation of alkyl radicals in the vapour phase from sodium vapour and alkyl halides,[†] e.g.

$$H_3C{\cdot}I + Na{\cdot} \rightarrow H_3C{\cdot} + NaI.$$

Radical reactions may be divided into four main categories. First, there are many simple reactions where radicals once formed merely combine to form saturated dimers, just as hydrogen atoms combine to form molecular hydrogen. Secondly, radicals may abstract atoms from normal molecules, forming a new radical and a saturated molecule; in some cases we may be interested in the formation of the new saturated molecule only, in others in the subsequent reactions of the new radicals. Thirdly, there are chain reactions in which the intermediates are radicals, the peroxide-catalysed addition of HBr to olefines being a good example; and fourthly, there is the substitution of aromatic compounds by radicals.

Simple recombination reactions

1. *The Kölbe reaction*

Just as atomic anions, such as Br^-, on electrolytic discharge give at the anode free atoms which recombine to molecules, so can anions of aliphatic carboxylic acids be discharged to give acyloxy radicals; the latter readily lose CO_2 to form alkyl radicals which dimerize.

$$R{\cdot}CO_2^- - ⓔ \rightarrow R{\cdot}CO_2{\cdot} \rightarrow R{\cdot} + CO_2$$

$$2R{\cdot} \rightarrow R{-}R$$

The mechanism follows from analogy; and also from the formation of triphenylmethyl peroxide when triphenylacetic acid is electrolysed[‡] in pyridine in presence of oxygen, indicating the formation of triphenylmethyl, and the analogous formation of known oxidation products of diphenylmethyl when diphenylacetic acid is electrolysed[§] in methanol-pyridine in presence of oxygen. Moreover, Fichter and Stenzl[||] found that the electrolysis of benzoic acid in pyridine gave a mixture of all three phenylpyridines, a result which proved that phenyl radicals were intermediates (cf. p. 278).

In the electrolysis of aliphatic acids, olefines and paraffins with the same number of carbon atoms as the parent alkyl appear as by-products. These are apparently formed by disproportionation of the intermediate alkyl radicals, e.g.

[†] For a full account of radical reactions in the gas phase see Steacie, *Atomic and Free Radical Reactions*, Reinhold, 1946.

[‡] Riccoboni, *Gazz.* 1940, **70**, 748.

[§] Hoek and Nauta, *Rec. trav. chim.* 1942, **61**, 845.

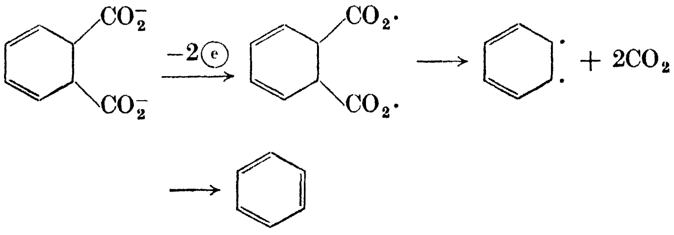
[||] Fichter and Stenzl, *Helv. Chim. Acta*, 1939, **22**, 970.

$$R\cdot CH_2\cdot CH_2\cdot CO_2^- \xrightarrow{-\textcircled{e}} R\cdot CH_2\cdot CH_2\cdot CO_2\cdot \rightarrow R\cdot CH_2\cdot CH_2\cdot + CO_2$$

$$2R\cdot CH_2\cdot CH_2\cdot \begin{array}{l} \rightarrow R\cdot CH{=}CH_2 + R\cdot CH_2\cdot CH_3 \\ \searrow R\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot R \end{array}$$

Bamford and Norrish† have shown that large alkyl radicals disproportionate rather than recombine; they prepared the radicals by photolysis of ketones in hot paraffin, when the alkyl radicals formed by photolysis attack the solvent and so primary recombination is repressed. The paraffin became unsaturated, showing that the large radicals so formed disproportionate, rather than recombine to larger paraffin molecules. The same effect is seen in vinyl polymerizations (next chapter). It is not altogether clear why radical combination occurs so readily in the Kölbe reaction; possibly the radicals combine by a surface reaction on the anode, being held there by their unsaturated centres until combination occurs. While the radical centres are held by the anode disproportionation will be sterically less favourable than combination.

An amusing Kölbe reaction was described recently:‡ electrolysis of salts of 1:2-dihydrophthalic acid gives benzene.



2. *The Wurtz reaction*

Sodium vapour undoubtedly reacts with alkyl halides in the gas phase to form alkyl radicals, but it is still uncertain whether or not such radicals are formed from sodium and halides in solution. It seems likely on balance that they are usually not formed. Morton and his collaborators§ have shown that sodium alkyls can be prepared in good yield from sodium powder and alkyl halides, and that they react with more alkyl halide to give not only the normal Wurtz product but also all the by-products obtained in the corresponding Wurtz reaction. Disproportionation is a simple $-S_2$ elimination under these conditions, and hence its occurrence in the Wurtz reaction is no indication that radicals are intermediates, e.g.

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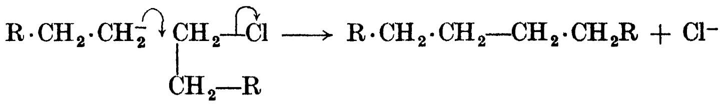
† *J.C.S.* 1938, 1531.

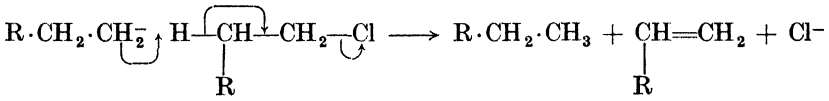
‡ Pasquinelli, *Anales asoc. quim. argentina*, 1943, **31**, 181.

§ *J.A.C.S.* 1942, **64**, 2240, 2242.

$$R\cdot CH_2\cdot CH_2Cl + 2Na \longrightarrow R\cdot CH_2\cdot CH_2^-Na^+ + NaCl$$



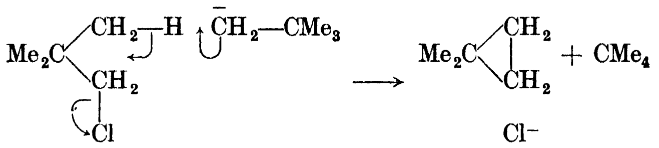
$$R\cdot CH_2\cdot CH_2^- \; \underset{|}{CH_2}(CH_2{-}R){-}Cl \longrightarrow R\cdot CH_2\cdot CH_2{-}CH_2\cdot CH_2R + Cl^-$$



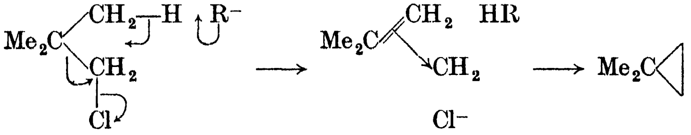
$$R\cdot CH_2\cdot CH_2^- \; H{-}\underset{R}{\underset{|}{CH}}{-}CH_2{-}Cl \longrightarrow R\cdot CH_2\cdot CH_3 + \underset{R}{\underset{|}{CH}}{=}CH_2 + Cl^-$$

The same may be true in the reaction of neopentyl chloride with sodium to give dimethylcyclopropane:†

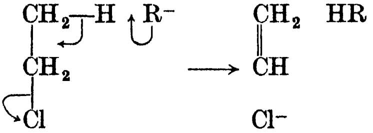
$$Me_3C\cdot CH_2Cl + 2Na \rightarrow Me_3C{-}CH_2^- \quad Na^+ \quad NaCl$$



In this case the mechanism would seem even more natural in the π-complex interpretation, although the product is probably not a π-complex (p. 157).



cf.



It is true that chlorobenzene gives benzene, diphenyl, *p*-terphenyl, and triphenylene when treated with sodium,‡ a result which may imply that phenyl radicals are intermediate; on the other hand, the Na+ group in sodium phenyl is one of the most powerful cationoid substituents known,§ and since sodium aryls are known to metallate aromatic nuclei, the mechanism may actually be:

$$PhCl + 2Na \longrightarrow Ph^-Na^+ + NaCl$$

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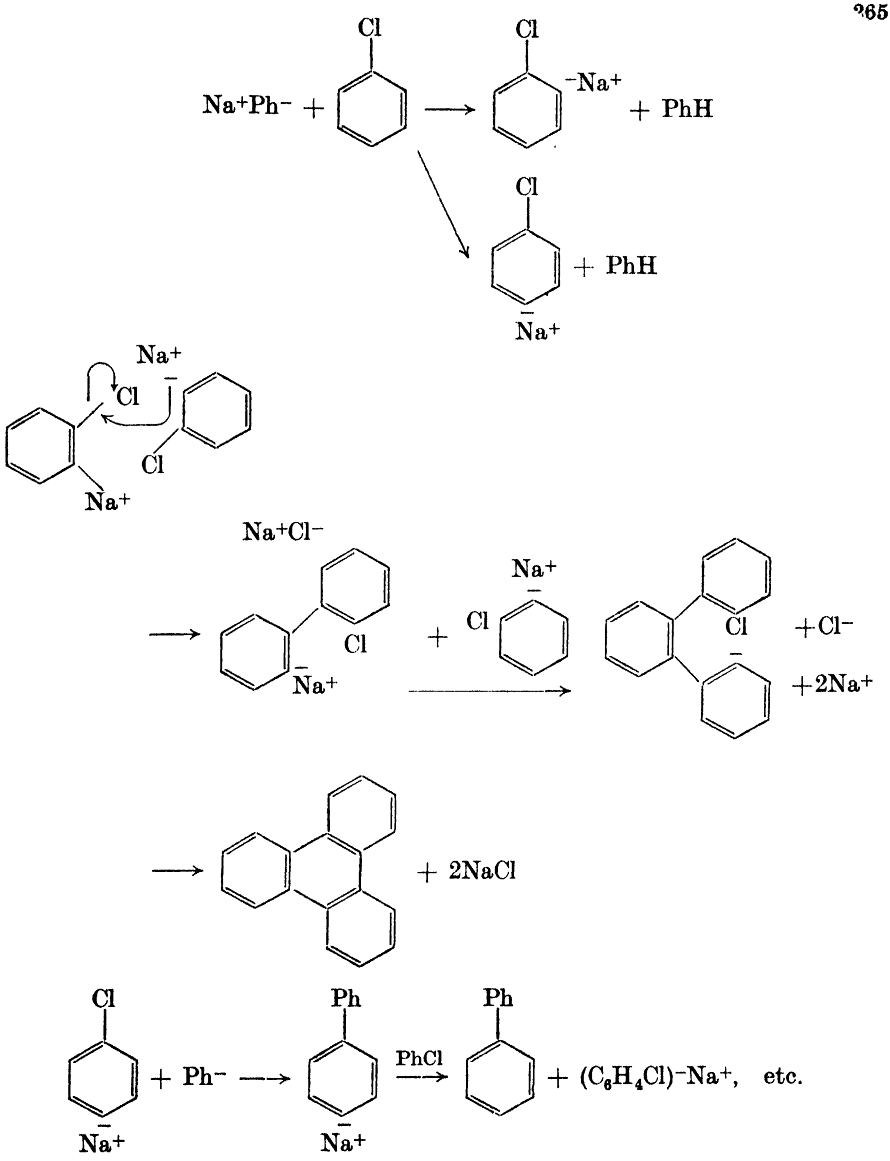
† Whitmore, Popkin, Bernstein, and Wilkins, *J.A.C.S.* 1941, **63**, 124, 2633.

‡ Bachman and Clarke, ibid. 1927, **49**, 2089.

§ Morton, Little, and Strong, ibid. 1943, **65**, 1339.



the cationoid Na$^+$ activating the chlorine to anionoid replacement, just as does the NO_2 in *o*- or *p*-nitrochlorobenzene.

All in all, the mechanism of the Wurtz reaction remains uncertain, but there is still no real evidence that it involves radical intermediates.

3. *Oxidative Kölbe reaction*

The removal of one electron from a carboxylate anion can be effected by oxidizing agents of high potential,† particularly persulphates. The resulting radicals then dimerize, disproportionate, etc., just as in the normal Kölbe reaction, though disproportionation seems to be more prominent than usual (cf. p. 261). The persulphate anion in this reaction behaves virtually as the radical SO_4^- ; and it is interesting that the electrosynthesis of persulphates undoubtedly proceeds via this radical, formed by partial discharge of $SO_4^=$ at the anode.

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† Fichter et al., *Helv. Chim. Acta*, **1933, 16,** 885; **1935, 18,** 704, 1276; **1936, 19, 149.**

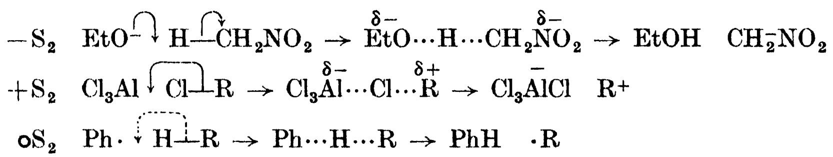
$$R{\cdot}CO_2^- + {\cdot}SO_4^- \rightarrow R{\cdot}CO_2{\cdot} + SO_4^=, \quad \text{etc.}$$

It is interesting also that esters are formed as by-products in both the normal and oxidative Kölbe reactions, presumably by combination of an alkyl and undissociated acyl radical; e.g.

$$\begin{aligned} &Et{\cdot}CO_2^- \xrightarrow{-ⓔ} Et{\cdot}CO_2{\cdot} \\ &Et{\cdot}CO_2{\cdot} \rightarrow Et{\cdot} + CO_2 \\ &Et{\cdot} + Et{\cdot}CO_2{\cdot} \rightarrow Et{\cdot}CO_2{\cdot}Et \end{aligned}$$

Radical replacement reactions

Just as an anion may abstract a proton from an acid, or a cationoid reagent such as $AlCl_3$ a halogen anion from a halide, so may a radical abstract an atom from a normal molecule to give a new radical. The latter reaction is essentially an S_2 replacement by a radical (oS_2) as the following parallel shows (dotted lines imply transfers of single electrons during reaction).



$$\begin{aligned} -S_2\quad & EtO^- \; H{-}CH_2NO_2 \rightarrow \overset{\delta-}{EtO}\cdots H\cdots CH_2\overset{\delta-}{NO_2} \rightarrow EtOH \quad CH_2^-NO_2 \\ +S_2\quad & Cl_3Al \; Cl{-}R \rightarrow Cl_3\overset{\delta-}{Al}\cdots Cl\cdots\overset{\delta+}{R} \rightarrow Cl_3\overset{-}{Al}Cl \quad R^+ \\ oS_2\quad & Ph{\cdot} \; H{-}R \rightarrow Ph\cdots H\cdots R \rightarrow PhH \quad {\cdot}R \end{aligned}$$

Reactions of this type were first observed by Wieland, Popper, and Seefried† in the decomposition of benzeneazotriphenylmethane, which on heating gives nitrogen and free triphenylmethyl, the latter being identified spectroscopically and as the peroxide. Since the Ph_3C group is eliminated as a radical, so must also be the phenyl, and when the reaction was carried out in light petroleum, benzene (but no diphenyl) was formed. The reaction must therefore be

$$\begin{aligned} Ph{-}N{=}N{-}CPh_3 &\rightarrow Ph{\cdot} + N_2 + {\cdot}CPh_3 \\ Ph{\cdot} + H{-}R &\rightarrow Ph{-}H + {\cdot}R \end{aligned}$$

followed by disproportionation or recombination of the radicals derived from the solvent.

Grieve and Hey‡ showed that the decomposition of other azo compounds likewise gives aryl radicals; the rate of nitrogen evolution is independent of the solvent, although the products of reaction vary in different solvents, and hence the first step must be a unimolecular decomposition of the azo compound. Moreover, the independence of the rate from the dielectric constant of the medium shows that the reaction is not ionic. The phenyl radicals abstract hydrogen atoms from paraffin solvents, halogen from alkyl halides, and substitute aromatic solvents (cf. p. 278). In the latter case the orientation of the products shows that attack is by radicals. N-Nitrosoacetanilide reacts similarly, presumably by a preliminary isomerization to benzene diazoacetate.

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† *Ber.* 1922, **55**, 1816.

‡ *J.C.S.* 1934, 1797; see Hey, *Ann. Rep. Chem. Soc.* 1940, **37**, 268; 1944, **41**, 181.

$$\mathrm{Ph{\cdot}N{=}N{\cdot}X} \rightarrow \mathrm{Ph\cdot} + \mathrm{N_2} + \mathrm{\cdot X} \quad (\mathrm{X} = \mathrm{OH, Cl, OAc}, \text{etc.})$$

$$\mathrm{Ph\cdot} + \mathrm{H{-}R} \rightarrow \mathrm{PhH} + \mathrm{R\cdot}$$

$$\mathrm{Ph\cdot} + \mathrm{CCl_4} \rightarrow \mathrm{PhCl} + \mathrm{\cdot CCl_3}, \quad \text{etc.}$$

The formation of radical intermediates has also been proved† by the formation of metal acetates when nitrosoacetanilide decomposes in presence of metals, such as lead, tin, copper, or mercury, which are not attacked by acetate ions or acetic acid under the same conditions.

It is interesting that phenyl radicals formed in these reactions show little tendency to combine, and it has been suggested that they differ qualitatively from aliphatic radicals. However, in the gas phase free phenyl radicals readily combine to form diphenyl,‡ so it is evident that their failure to react likewise in solution is due not to inability to combine but to their exceptional reactivity. Aryl radicals at once attack aliphatic solvents in the cold to form benzene derivatives and alphyl radicals, while aromatic solvents are immediately arylated. The analogous reactions of alphyl radicals occur much less readily, and so alphyl radicals, unlike aryl radicals, can survive long enough in such solutions to react with one another. This effect may be correlated with the greater strength of C—X bonds formed by carbon in an aromatic system compared with similar bonds in aliphatic compounds. Incidentally much diphenyl is formed when etheral phenylmagnesium bromide is electrolysed,§ and part at least of this may derive from combination of free phenyl radicals formed by discharge of phenyl anions at the anode; although the formation of diphenyl by phenylation of benzene produced in a preliminary attack of Ph on the solvent cannot be excluded.

Bamford and Norrish‖ have shown that alkyl radicals will rapidly attack paraffin solvents at temperatures above 80°, behaving just as aryl radicals do in the cold. The activation energy for the reaction of alphyl radicals (12·3 Cals.) is evidently much greater than that for aryl radicals. Moreover, alphyl radicals readily abstract halogen from solvents such as $\mathrm{CCl_4}$ or RI in the cold; these reactions occur more readily since the (C—halogen) bonds are weaker than C—H and hence $\mathrm{oS_2}$ replacements of the type

$$\mathrm{R\cdot} + \mathrm{ClCCl_3} \rightarrow \mathrm{R{-}Cl} + \mathrm{\cdot CCl_3}$$

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† Waters, *J.C.S.* 1937, 2007.

‡ Horn and Polanyi, *Z. phys. Chem.* 1934, B **25**, 151; Dull and Simons, *J.A.C.S.* 1933, **55**, 3898, 4328; Leighton and Mortensen, ibid. 1936, **58**, 448.

§ Evans, Pearson, and Braithwaite, ibid. 1941, **63**, 2574.

‖ *J.C.S.* 1938, 1531, 1540.

occur more readily than corresponding reactions with hydrocarbons. Other radical replacement reactions will be discussed later (p. 291).

Decomposition of acyl peroxides

Radicals can also be formed by thermal decomposition of acyl peroxides. The O—O bond is a weak one (bond-energy 64 Cals.), and since acyloxy radicals are derived from mesomeric acylate anions by loss of one electron and are therefore themselves mesomeric, the energy required to break the O—O bond in a diacyl peroxide is even less (30–40 Cals.). The decomposition of an acyl peroxide gives the same acyloxy radicals that are formed in the Kölbe reaction, and their subsequent reactions are similar, carbon dioxide, paraffins, and olefines being formed. Decomposition of benzoyl peroxide likewise gives benzoyloxy radicals which decompose into carbon dioxide and free phenyl, and the subsequent reactions parallel those of phenyl liberated from the azo derivatives mentioned above.

Effects of structure

The case of the replacement reaction

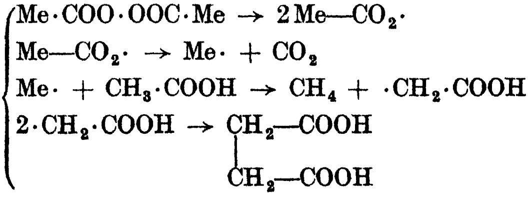
$$\mathrm{R}\cdot + \mathrm{Cl{-\!\!-}R'} \rightarrow \mathrm{R{-\!\!-}Cl} + \cdot\mathrm{R'}$$

will depend on the stability of the transition state,

$$\mathrm{R}\cdots\mathrm{Cl}\cdots\mathrm{R'}$$

in which both R and R′ have partial radical character. Following the usual principles we may expect radical-stabilizing groups in R to retard reaction (since R is less a radical in the transition state than initially) and in R′ to accelerate it. Since any substituents stabilize radicals but positive substituents and E-substituents do so most strongly, we may deduce that the oS_2 reaction will be favoured by positive and by E-active substituents in R′. There is no quantitative evidence available, the rates of radical reactions being very difficult to measure on account of the numerous side-reactions which reactive radicals undergo, but the qualitative evidence supports these conclusions. Thus decomposition of alkylcarbonyl peroxides in $\mathrm{CCl_4}$ gives alkyl chlorides in place of the usual hydrocarbons since the $\cdot\mathrm{CCl_3}$ radical is stabilized by substitution with chlorine; and decomposition of acetyl peroxide in acetic acid gives succinic acid:†

$$\begin{cases} \mathrm{R\cdot CO\cdot O\cdot O\cdot CO\cdot R} \rightarrow 2\mathrm{R{-\!\!-}CO_2}\cdot \\ \mathrm{R{-\!\!-}CO_2}\cdot \rightarrow \mathrm{R}\cdot + \mathrm{CO_2} \\ \mathrm{R}\cdot + \mathrm{CCl_4} \rightarrow \mathrm{R{-\!\!-}Cl} + \cdot\mathrm{CCl_3} \end{cases}$$



$$\begin{cases} \mathrm{Me\cdot COO\cdot OOC\cdot Me} \rightarrow 2\mathrm{Me{-\!\!-}CO_2}\cdot \\ \mathrm{Me{-\!\!-}CO_2}\cdot \rightarrow \mathrm{Me}\cdot + \mathrm{CO_2} \\ \mathrm{Me}\cdot + \mathrm{CH_3\cdot COOH} \rightarrow \mathrm{CH_4} + \cdot\mathrm{CH_2\cdot COOH} \\ 2\cdot\mathrm{CH_2\cdot COOH} \rightarrow \begin{array}{l} \mathrm{CH_2{-\!\!-}COOH} \\ | \\ \mathrm{CH_2{-\!\!-}COOH} \end{array} \end{cases}$$

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† Kharasch and Gladstone, *J.A.C.S.* 1943, **65**, 15.

In the former case substitution of the alkyl in the peroxide by methyl or phenyl lowers the activity of the resulting alkyl radical and hence neither pivalyl peroxide ($Me_3C\cdot COO\cdot OOC\cdot CMe_3$) nor phenylacetyl peroxide reacts with hot carbon tetrachloride to give corresponding alkyl chlorides.[†]

Kharasch[†] has used this type of reaction to show that no rearrangement occurs when propyl or *iso*-propyl radicals are set free in solution, butyryl and *iso*-butyryl peroxides giving only *n*-propyl and *iso*-propyl chlorides respectively on decomposition in CCl_4.

$$(Pr_\alpha\cdot COO)_2 \rightarrow 2Pr_\alpha\cdot CO_2\cdot \rightarrow 2Pr_\alpha\cdot + 2CO_2$$

$$Pr_\alpha\cdot + CCl_4 \rightarrow Pr_\alpha Cl + \cdot CCl_3$$

$$(Pr_\beta\cdot COO)_2 \rightarrow 2Pr_\beta\cdot CO_2\cdot \rightarrow 2Pr_\beta\cdot + 2CO_2$$

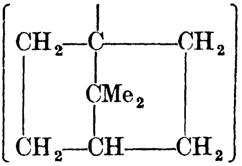
$$Pr_\beta\cdot + CCl_4 \rightarrow Pr_\beta Cl + \cdot CCl_3$$

The *n*-propyl cation rearranges to Me_2CH^+ very readily (p. 209), but radicals evidently do not easily undergo pinacol-type rearrangements. This is to be expected if the rearrangements take place via π-complexes, since a radical contains one electron too many to form a stable π-complex.

Kharasch, Engelmann, and Urry[‡] have found that 1-apocamphylcarbonyl peroxide (I) is unusually stable, and that its decomposition in CCl_4 gives the following products:

$$\underset{(I)}{(RCOO)_2} \xrightarrow{CCl_4} \underset{36\%}{RCl} + \underset{9\%}{R_2} + \underset{50\%}{R\cdot COOR} + \underset{5\%}{R\cdot COOH} + C_2Cl_6$$

R =



The apocamphyl radical must therefore be less stable and so more reactive than *tert*-butyl, which does not attack the solvent under these conditions. The normal configuration of free methyl is probably planar (p. 7), so the inferior stability of apocamphyl is presumably due to the fact that its ring-structure prevents the trivalent carbon from adopting a planar configuration. The actual course of the reaction is interesting and it has been misinterpreted by Kharasch. Unquestionably the lower stability of the apocamphyl radical lowers the rate of decomposition of the apocamphylcarboxyl radicals first formed; moreover, the apocamphyl radical, although more reactive than *tert*-butyl, is still relatively inert. Hence primary recombination (p. 255) of the $R\cdot COO\cdot$ radicals predominates at low temperatures, regenerating the peroxide, which therefore appears to be unusually stable. The stability is of the same kind as that shown by liquid acetone to ultra-violet light (ibid.). At higher temperatures, apocamphylcarboxyl radicals decompose to CO_2 and apocamphyl radicals; in most cases only one of the pair of acylate radicals formed from one peroxide molecule will decompose, and primary recombination of the resulting pair of radicals gives the ester (which is the main product of the reaction). In some cases both acylate radicals decompose, and primary recombination of the resulting apocamphyl radicals gives a small amount of diapocamphyl. The apocamphyl chloride and C_2Cl_6 are of course formed by attack on the solvent, and the apocamphane carboxylic acid by removal of hydrogen from apocamphane derivatives by the acid radical. The complete mechanism is:

[†] Kharasch, Kane, and Brown, ibid. 1942, **64**, 1621.

[‡] *J.A.C.S.* 1943, **65**, 2428.

$$(R\cdot COO)_2 \rightarrow 2R\cdot COO\cdot$$

$$\left.\begin{array}{l}
2R\cdot COO\cdot \rightarrow (R\cdot COO)_2\\
2R\cdot COO\cdot \rightarrow \underset{\displaystyle\downarrow}{R\cdot COO\cdot} + R\cdot + CO_2 \rightarrow R\cdot COOR\\
\qquad\qquad\qquad 2R\cdot + 2CO_2 \rightarrow R{-}R
\end{array}\right\}\ \text{primary recombination}$$

$$R\cdot + CCl_4 \rightarrow R{-}Cl + \cdot CCl_3$$

$$R\cdot COO\cdot + R'H \rightarrow R\cdot COOH$$

$$2\ \cdot CCl_3 \rightarrow C_2Cl_6$$

This reaction in detail shows clearly the need for keeping the Franck-Rabinowitsch principle in mind when one is considering the mechanisms of radical reactions. The formation of esters in other acyl peroxide decompositions (e.g. $(PhCOO)_2$) is undoubtedly due to primary recombination, and the primary recombination of acyloxy radicals to the acyl peroxide has also been demonstrated by a study of the kinetics of peroxide-catalysed polymerizations.

Abnormal Grignard reactions involving radicals

Kharasch and his collaborators have shown that small proportions of certain metal halides, especially cobalt chloride, $CoCl_2$, profoundly alter the course of many Grignard reactions. The mechanism was established by an examination† of the reaction between phenylmagnesium bromide and various alkyl halides. In the absence of $CoCl_2$ the reaction was slow and no gas was evolved, but in presence of 3–5 molecules per cent. of $CoCl_2$, a vigorous reaction occurred, and diphenyl and hydrocarbon gases were formed in equivalent amounts with very little alkylbenzene. The hydrocarbon gases corresponded to those formed by combination or (mainly) disproportionation of the alkyl radicals. The only reasonable mechanism involves the intermediate formation of cobalt subchloride.

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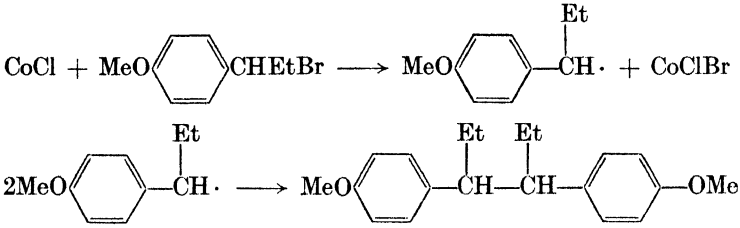
† Kharasch, Lewis, and Reynolds, *J.A.C.S.* 1943, **65**, 493; see Kharasch and Fields, ibid. 1941, **63**, 2316.

Free phenyl radicals cannot be formed, since otherwise benzene and terphenyl would be found in the products:

$$\mathrm{PhMgBr} + \mathrm{CoCl_2} \rightarrow \mathrm{PhCoCl} + \mathrm{MgClBr}$$
$$2\mathrm{PhCoCl} \rightarrow \mathrm{Ph{-}Ph} + 2\mathrm{CoCl}$$
$$\mathrm{CoCl} + \mathrm{RCl} \rightarrow \mathrm{CoCl_2} + \mathrm{R.}$$

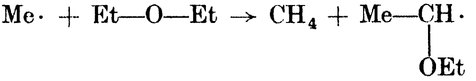
This reaction has been used to prepare hexoestrol dimethyl ether from anethole hydrobromide.†

$$\mathrm{PhMgBr} + \mathrm{CoCl_2} \longrightarrow \mathrm{PhCoCl} + \mathrm{MgClBr}$$
$$2\mathrm{PhCoCl} \longrightarrow \mathrm{Ph_2} + 2\mathrm{CoCl}$$



Methylmagnesium bromide reacts likewise with $\mathrm{CoCl_2}$, except that the intermediate methyl cobaltochloride seems to decompose spontaneously to methyl radicals and CoCl. Thus a considerable amount of methane is formed in the reaction with cyclohexyl chloride in ether, together with ethylene; these presumably arise from attack on the solvent. (Kharasch gives a slightly different and less probable scheme for this attack.)

$$\mathrm{MeMgBr} + \mathrm{CoCl_2} \rightarrow \mathrm{Me\cdot} + \mathrm{CoCl} + \mathrm{MgClBr}$$



$$\mathrm{Me\cdot} + \mathrm{Et{-}O{-}Et} \rightarrow \mathrm{CH_4} + \mathrm{Me{-}}\underset{\displaystyle \mathrm{OEt}}{\mathrm{CH}}\mathrm{\cdot}$$

$$\mathrm{Me{-}\dot{C}H{-}OEt} \rightarrow \mathrm{MeCHO} + \mathrm{Et\cdot}$$
$$2\mathrm{Et\cdot} \rightarrow \mathrm{C_2H_4} + \mathrm{C_2H_6}$$

The radical $\mathrm{R{-}\dot{C}H{-}OEt}$ is known to decompose easily to free ethyl and aldehyde, from the reactions of alkyl radicals liberated in ethers by electrolysis of Grignard reagents. (This reaction resembles the Kölbe synthesis.) If the electrolysis is carried out in ethyl ether, products of disproportionation of ethyl and carbinols derived from the acetaldehyde are formed.‡

$$\mathrm{Ph^-Mg^+Br} \xrightarrow{\text{electrolyse}} \mathrm{Ph\cdot}$$
$$\mathrm{Ph\cdot} + \mathrm{Et_2O} \rightarrow \mathrm{PhH} + \mathrm{CH_3{\cdot}\dot{C}H{\cdot}OEt}$$
$$\mathrm{CH_3{\cdot}\dot{C}H{\cdot}OEt} \rightarrow \mathrm{CH_3CHO} + \mathrm{Et\cdot}$$
$$2\mathrm{Et\cdot} \rightarrow \mathrm{C_2H_4} + \mathrm{C_2H_6}$$
$$\mathrm{PhMgBr} + \mathrm{CH_3CHO} \rightarrow \mathrm{Ph{\cdot}CHOH{\cdot}Me} \rightarrow \mathrm{Ph{\cdot}CH{=}CH_2}$$

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† Kharasch and Kleiman, ibid. 1943, **65**, 491.

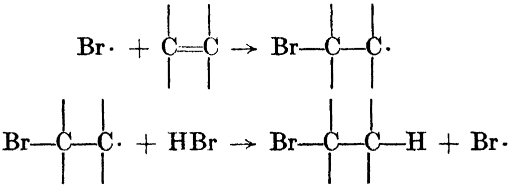
‡ Evans, Pearson, and Braithwaite, ibid. 1941, **63**, 2574.

Other ethers react likewise. It is interesting that electrolysis of methylmagnesium iodide in butyl ether gives products derived from butyraldehyde and free butyl.[†] Methyl radicals do not attack paraffin hydrocarbons in the cold, so the α-alkoxyalkyl radical must be more easily formed, i.e. more stable, than alkyl. This would be expected, since alkoxyl, being strongly $-E$ and quite strongly $+I$, should be a fairly efficient radical stabilizer.

Radical-chain reactions

Since a radical is by definition a molecule containing an odd electron, any reaction with a 'normal' molecule (in which the electrons are all paired) must give another radical. Hence a radical, once formed, may initiate a long 'chain' of reactions, each of which generates a new radical. The chain will be terminated only by some process which removes radicals; either mutual reaction of two radicals to give normal molecules (by combination or disproportionation), or the formation of a mesomeric radical which is stable enough not to undergo further reaction.

The reaction chain normally consists for the most part of a repeating cycle of reactions in which the radical which initiated the cycle is regenerated at the end. A simple example was given earlier, the peroxide-catalysed addition of HBr to olefines where the main part of the chain consists of the reactions:



$$\mathrm{Br}\cdot + \mathrm{C{=}C} \rightarrow \mathrm{Br{-}C{-}C}\cdot$$

$$\mathrm{Br{-}C{-}C}\cdot + \mathrm{HBr} \rightarrow \mathrm{Br{-}C{-}C{-}H} + \mathrm{Br}\cdot$$

The bromine atom virtually catalyses the combination of olefine and HBr, and one bromine atom may bring about the combination of a very large number of molecules of the reactant before the chain is terminated, for instance, by the mutual combination of Br atoms to $\mathrm{Br_2}$.

Theoretically, of course, ionic chain reactions should be possible, but in practice they are rarely observed. Ions are 'normal' molecules with all their electrons paired, and hence they can nearly always form inert products by reaction with normal molecules. A radical can only fail to give another reactive radical in a reaction if the other reactant is also a radical or one of a comparatively small group of *inhibitors*; an inhibitor is a substance which can react with radicals to give relatively inert mesomeric radicals and so break radical chains.

Radical-chain reactions show several very characteristic features. Firstly, they are catalysed by free radicals or substances which can give free radicals under the conditions of reaction (e.g. benzoyl peroxide). Secondly, they are inhibited by compounds such as quinone or picric acid which are known to react easily with radicals; such inhibitors break the reaction chains by removing the radical intermediates. These two effects are shown qualitatively by a great sensitivity of reaction rate to the purity of the reactants; oxygen in particular can produce capricious effects since, being virtually a diradical, it may act as either a catalyst or an inhibitor. It should be noted that radical catalysis is a necessary, but not a sufficient, criterion that a given reaction takes place by a radical-chain mechanism (cf. p. 132). It is necessary also to demonstrate that the reaction can be completely inhibited. It may be added that the length of chains, that is, the numbers of cycles of elementary reactions that are brought about by single radicals, are frequently very large and generally > 100. Hence inhibitors reduce the rates of such reactions by a very large factor.

[†] Evans and Field, *J.A.C.S.* 1936, **58**, 720, 2284; cf. Evans and Braithwaite, ibid. 1939, **61**, 898.

A third criterion is provided in photochemical reactions by the very large quantum yields of chain reactions. A single quantum of light can be absorbed only by a single molecule, and hence in a non-chain reaction one molecule at most reacts per quantum absorbed. The actual quantum yield, the number of molecules reacting per quantum, is generally less than one because the reactant molecule may get rid of the energy it absorbs in other ways, e.g. by re-emission of light (fluorescence) or by collision with solvent molecules. In a few cases quantum yields of 2 are observed in the absence of chains, but these can always be ascribed to simple secondary reactions. Thus the primary photodecomposition of HI gives H· and I· atoms, and the former can decompose a second HI molecule.

$$\mathrm{H{-}I} \xrightarrow{h\nu} \mathrm{H\cdot} + \mathrm{I\cdot}$$

$$\mathrm{H\cdot} + \mathrm{HI} \rightarrow \mathrm{H_2} + \mathrm{I\cdot}$$

$$2\mathrm{I\cdot} \rightarrow \mathrm{I_2}$$

In a chain reaction, however, the radicals formed in the primary decomposition may bring about the combination of thousands or millions of molecules of the reactants. Hence although the quantum yield of the primary act is $\leqslant 1$, the apparent quantum yield will be very large. Conversely a quantum yield $\gg 1$ indicates a chain reaction.

A fourth criterion of chain reactions is the existence of *induction periods*. In the stationary state of such a reaction, chains of all lengths will be present, scattered statistically about the mean length. Initially there are no chains. Since each complete chain involves a very large number of individual steps, it takes a finite time for the equilibrium state to be established. Hence the rate of reaction takes a finite time to reach its steady value, after the formation of radicals has begun. This effect has rarely been established since it is usually masked by the presence of inhibitors; if traces of inhibitor are present, the rate of reaction will increase steadily with time as the inhibitors are removed by reaction with radicals, and it is difficult to establish that an observed 'induction period' is not due to this effect.

Kinetics of chain reactions

Chain reactions can be divided into three stages: initiation, the formation of radicals; propagation, the repeating cycle of reactions, usually two in number; and termination, the removal of radicals. The termination reaction in the liquid phase is always a bimolecular combination or disproportionation of radicals, or a reaction of radicals with an inhibitor. We may express these conclusions in the following idealized scheme.

$$\begin{array}{lll}
\text{Initiation} & ? \rightarrow \alpha \quad . \quad . \quad . \quad . & \text{rate } k_1 \\
\text{Propagation} & \left\{\begin{array}{l} \alpha + \mathrm{A} \rightarrow \beta + \mathrm{P} \quad . \quad . \\ \beta + \mathrm{B} \rightarrow \alpha + \mathrm{Q} \quad . \quad . \end{array}\right. & \begin{array}{l} ,, \ k_2[\alpha][\mathrm{A}] \\ ,, \ k_3[\beta][\mathrm{B}] \end{array} \\
\text{Termination} & \left\{\begin{array}{l} 2\alpha \rightarrow \ ? \quad . \quad . \quad . \quad . \\ \alpha + \beta \rightarrow \ ? \quad . \quad . \quad . \\ 2\beta \rightarrow \ ? \quad . \quad . \quad . \quad . \end{array}\right. & \begin{array}{l} ,, \ k_4[\alpha]^2 \\ ,, \ k_5[\alpha][\beta] \\ ,, \ k_6[\beta]^2 \end{array}
\end{array}$$

A, B are the reactants which are converted to the products P, Q in the propagation phase; α, β are the radical intermediates or *chain carriers.* Applying the stationary state method, we have

$$\frac{d[\alpha]}{dt} = k_1 - k_2[\alpha][\mathrm{A}] + k_3[\beta][\mathrm{B}] - k_4[\alpha]^2 - k_5[\alpha][\beta] = 0,$$

$$\frac{d[\beta]}{dt} = k_2[\alpha][\mathrm{A}] - k_3[\beta][\mathrm{B}] - k_5[\alpha][\beta] - k_6[\beta]^2 = 0.$$

Unfortunately an attempt to solve these equations directly gives a quartic equation for (α) or (β), and this has no simple solution. The equations can be solved if we make the reasonable assumption that the rate constant for the reaction between α and β is the geometric mean of those for the reactions of α with α and of β with β; i.e. that $k_4^2 = k_3 k_5$. We then find

$$[\alpha] = \frac{k_3[\mathrm{B}]\sqrt{k_1}}{k_2[\mathrm{A}]\sqrt{k_6} + k_3[\mathrm{B}]\sqrt{k_4} + k_5\sqrt{k_1}}; \qquad [\beta] = \frac{k_2[\mathrm{A}]\sqrt{k_1}}{k_2[\mathrm{A}]\sqrt{k_6} + k_3[\mathrm{B}]\sqrt{k_4} + k_5\sqrt{k_1}}$$

and hence
$$\frac{d[\mathrm{P}]}{dt} = \frac{d[\mathrm{Q}]}{dt} = \frac{k_2 k_3[\mathrm{A}][\mathrm{B}]\sqrt{k_1}}{k_2[\mathrm{A}]\sqrt{k_6} + k_3[\mathrm{B}]\sqrt{k_4} + k_5\sqrt{k_1}}.$$

If the chains are long, the rate at which radicals are formed must be small compared with the rates of the propagation reactions. It is easily shown that the last term in the denominator is then negligible and so the overall rate is given by

$$\frac{d[\mathrm{P}]}{dt} = \frac{d[\mathrm{Q}]}{dt} = \frac{k_2 k_3[\mathrm{A}][\mathrm{B}]\sqrt{k_1}}{k_2[\mathrm{A}]\sqrt{k_6} + k_3[\mathrm{B}]\sqrt{k_4}}. \qquad \text{(I)}$$

The rate is thus proportional to the square root of the rate (k_1) at which radicals are formed. Also if $k_4 \ll k_6$, the rate reduces to $(k_3/\sqrt{k_6})[\mathrm{B}]\sqrt{k_1}$: and if $k_6 \gg k_4$, to $(k_2/\sqrt{k_4})[\mathrm{A}]\sqrt{k_1}$. If $k_4 \sim k_6$, or if $k_4 = k_6 = 0$ and k_5 is finite, the rate can be expressed approximately as $k'[\mathrm{A}]^{\frac{1}{2}}[\mathrm{B}]^{\frac{1}{2}}\sqrt{k_1}$, where k' is a constant. Thus although the kinetic analysis is somewhat complex, the observed rate of reaction is likely to follow quite simple laws. The most striking feature is the dependence of rate on the square root of the rate of chain-initiation. This relation is characteristic of all chain reactions where termination takes place by bimolecular reaction of the chain carriers.

Halogenation of paraffins

It has long been known that paraffins are chlorinated and brominated at moderate temperatures in presence of light. The reactions are very easily inhibited, their rates are difficult to reproduce, and their quantum yields are very high. There can therefore be little doubt that they occur by chain mechanisms, the chains being started by halogen atoms formed by photodissociation of free halogen. It is known from spectroscopic evidence that light capable of effecting the halogenation can split halogen molecules into atoms. Moreover, in a photochemical chain reaction the rate of chain-starting is equal to $\phi \cdot I_{\text{abs}}$, where I_{abs} is the amount of light absorbed and ϕ is the quantum yield. The majority of these substitution reactions take place at rates proportional to the square root of the absorbed light intensity, as the kinetic scheme above requires. The mechanism is presumably

$$\mathrm{X_2} \xrightarrow{h\nu} \mathrm{2X\cdot} \tag{1}$$

$$\mathrm{X\cdot + H{-}R \rightarrow X{-}H + R\cdot} \tag{2}$$

$$\mathrm{R\cdot + X_2 \rightarrow R{-}X + X\cdot} \tag{3}$$

$$\mathrm{2X\cdot \rightarrow X_2} \tag{4}$$

$$\mathrm{X\cdot + R\cdot \rightarrow RX} \tag{5}$$

$$\mathrm{2R\cdot \rightarrow R_2} \tag{6}$$

Comparison with (I) indicates that the overall rate should be given by

$$\frac{d[\mathrm{RX}]}{dt} = \frac{k_2 k_3[\mathrm{X_2}]\,[\mathrm{RH}](\phi I_{\text{abs}})^{\frac{1}{2}}}{k_2[\mathrm{RH}]\sqrt{k_6}+k_3[\mathrm{X_2}]\sqrt{k_4}}.$$

Most chlorinations† have rates proportional to the halogen concentration and independent of substrate; there the second term in the denominator must be negligible. But the rate of photohalogenation of formic acid is given‡ by $k[\mathrm{HCOOH}](I)^{\frac{1}{2}}$, the reactions being

$$\mathrm{Cl_2} \xrightarrow{h\nu} \mathrm{2Cl\cdot}$$

$$\mathrm{Cl\cdot + HCOOH \rightarrow HCl + \cdot COOH}$$

$$\mathrm{Cl_2 + \cdot COOH \rightarrow Cl\cdot + HCl + CO_2}$$

$$\mathrm{2Cl\cdot \rightarrow Cl_2}$$

$$\mathrm{Cl\cdot + HOOC\cdot \rightarrow HCl + CO_2}$$

$$\mathrm{2HOOC\cdot \rightarrow H_2 + 2CO_2}$$

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† See Steacie (p. 256) for a general survey.

‡ West and Rollefson, *J.A.C.S.* 1936, 58, 2140.

Here $k_3\sqrt{k_4} \gg k_2\sqrt{k_6}$. And the photochlorination of hexadecane in CCl_4 takes place at a rate given by $k[C_{16}H_{34}]^{\frac{1}{2}}[Cl_2]^{\frac{1}{2}}(I)^{\frac{1}{2}}$ at high chlorine concentrations;† all three modes of termination are then of comparable importance. There can therefore be little doubt that photohalogenation does take place by the chain mechanism given above, since it obeys exactly the expected kinetic laws.

Kharasch and Brown‡ have reported a number of analogous chlorinations brought about by sulphuryl chloride in presence of peroxide catalysts. No reaction takes place in the absence of catalyst, and the orientation of the product is little affected by substituents which would decisively control the course of an ionic reaction. Hence a radical chain again seems very probable. The detailed mechanism is presumably

$$\text{Initiation}\ \left\{\begin{array}{l}(PhCOO)_2 \rightarrow 2Ph\cdot + 2CO_2\\ Ph\cdot + SO_2Cl_2 \rightarrow PhCl + \cdot SO_2Cl\\ \cdot SO_2Cl \rightarrow SO_2 + Cl\cdot\end{array}\right.$$

$$\text{Propagation}\ \left\{\begin{array}{l}Cl\cdot + R\text{—}H \rightarrow HCl + R\cdot\\ R\cdot + SO_2Cl_2 \rightarrow RCl + \cdot SO_2Cl\\ \cdot SO_2Cl \rightarrow SO_2 + Cl\cdot\end{array}\right.$$

$$\text{Termination}\ \left\{\begin{array}{l}2Cl\cdot \rightarrow Cl_2\\ Cl\cdot + R\cdot \rightarrow RCl\\ 2R\cdot \rightarrow R_2\cdot,\quad \text{etc.}\end{array}\right.$$

With sulphuryl chloride and pyridine in light, hydrocarbons give sulphonyl chlorides.§ Since chlorination of heptane in presence of SO_2 gives a sulphonyl chloride,|| the mechanism is probably

$$\left\{\begin{array}{l}SO_2Cl_2 \xrightarrow{\text{pyridine}} SO_2 + Cl_2\\ Cl_2 \xrightarrow{h\nu} 2Cl\cdot\end{array}\right.$$

$$\left\{\begin{array}{l}Cl\cdot + RH \rightarrow R\cdot + HCl\\ R\cdot + SO_2 \rightarrow R\cdot SO_2\cdot\\ RSO_2\cdot + Cl_2 \rightarrow R\cdot SO_2Cl + Cl\cdot,\quad \text{etc.}\end{array}\right.$$

Other very similar substitution reactions are observed with oxalyl chloride in presence of peroxide catalysts or light.†† In both cases carboxylic acid chlorides are formed, and no reaction occurs in the absence of light or catalyst. The mechanism is presumably

$$\left\{\begin{array}{l}(PhCOO)_2 \rightarrow 2Ph\cdot + 2CO_2\\ Ph\cdot + (COCl)_2 \rightarrow PhCl + CO + \cdot COCl\end{array}\right.$$

† Stauff, *Z. Elektrochem.* 1942, **48**, 550.

‡ Kharasch and Brown, *J.A.C.S.* 1939, **61**, 2142; 1940, **62**, 2393, 3435.

§ Kharasch and Reid, ibid. 1939, **61**, 3089.

|| Stauff, *Z. Elektrochem.* 1942, **48**, 550.

†† Kharasch and Brown, *J.A.C.S.* 1940, **62**, 454.

or $$(\mathrm{COCl})_2 \xrightarrow{h\nu} 2\cdot\mathrm{COCl}, \quad \text{or} \quad \cdot\mathrm{Cl} + \mathrm{CO} + \cdot\mathrm{COCl}$$

and then $$\begin{cases} \cdot\mathrm{COCl} + \mathrm{RH} \rightarrow \mathrm{R}\cdot + \mathrm{HCl} + \mathrm{CO} \\ \mathrm{R}\cdot + (\mathrm{COCl})_2 \rightarrow \mathrm{R}\cdot\mathrm{COCl} + \cdot\mathrm{COCl} \end{cases}$$

with the usual bimolecular termination.

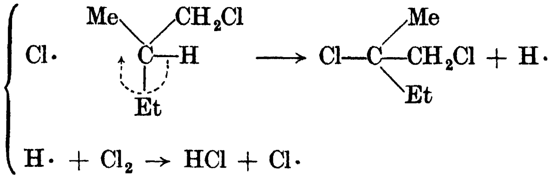
It may be added that information cannot usually be gained from isolation of the termination products, since if the chains are long they will be formed in amounts too small to isolate. When they can be isolated, they are found to conform to the general reaction schemes given above.

As a general rule, substitution can occur in more than one way. Since alkyl radicals do not rearrange (p. 263), the relative amounts of the various products will depend on the relative rates at which the corresponding alkyl radicals are formed, that is, the relative rates of reactions of the type $\mathrm{X}\cdot + \mathrm{RH} \rightarrow \mathrm{XH} + \mathrm{R}\cdot$. The rate of such a reaction will be greater, the more stable the radical $\mathrm{R}\cdot$. We should therefore expect hydrogen atoms in a hydrocarbon to be attacked in the order *tert* > *sec* > *prim*. This order of orientation is observed. We have assumed throughout that atoms or radicals react with complex molecules by removing peripheral atoms rather than by replacing groups; this would be expected on general grounds since radical reactions generally have very low activation energies and are very fast (no forces due to electrostatic interaction of ions being involved), while a reaction of the type

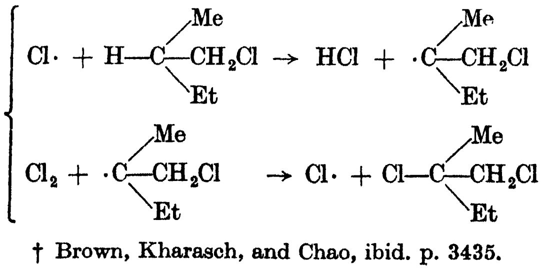
$$\mathrm{Cl}\cdot \; \mathrm{CH_3{-}CH_3} \rightarrow \mathrm{Cl{-}CH_3} + \mathrm{CH_3}\cdot$$

would have to take place by the inversion mechanism (p. 63) and the activation energy would doubtless be considerable.

Both these points are illustrated by the photochlorination of optically active primary amyl chloride to inactive 1:2-dichloro-2-methylbutane.† Obviously C—C fission would give lower alkyl halides, while substitution by the inversion mechanism



would give an optically active dichloride. In the alternative mechanism


Cl· + H—C—CH₂Cl → HCl + ·C—CH₂Cl
Me
Et
Cl₂ + ·C—CH₂Cl → Cl· + Cl—C—CH₂Cl
Me
Et

---

† Brown, Kharasch, and Chao, ibid. p. 3435.

the intermediate methyl radical would at once racemize. Moreover, attack takes place preferentially at the tertiary C—H, as we would expect, since *tert*-alkyl radicals are more stable than primary or secondary ones.

Addition to olefines

The peroxide-catalysed addition of HBr to olefines has already been mentioned. It is now known that many other compounds will add readily to olefines under conditions of radical catalysis. Thus halogens do not react appreciably with olefines in light petroleum by the normal ionic mechanism, the solvent being non-polar, but in light or in presence of peroxides addition readily occurs. The same is true of addition in the vapour phase, when allowance is made for the surface-catalysed reaction. The photochemical additions have very large quantum yields and are therefore undoubtedly chain reactions; they are, moreover, subject to inhibition, e.g. by oxygen. The rates† are proportional to $(I_{\text{abs}})^{\frac{1}{2}}$, and the kinetics in general resemble closely those of the halogenation reactions mentioned above. The mechanism is undoubtedly

$$Cl_2 \xrightarrow{h\nu} 2Cl\cdot$$

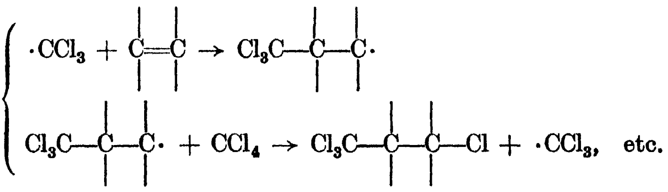
$$Cl\cdot + CR_2{=}CR_2 \rightarrow Cl\cdot CR_2\cdot \dot{C}R_2$$

$$ClCR_2{-}\dot{C}R_2 + Cl_2 \rightarrow ClCR_2\cdot CR_2Cl + Cl\cdot$$

with the usual bimolecular termination reactions.

The addition of other compounds to olefines has not been studied kinetically, but the qualitative evidence strongly supports similar mechanisms for them. Thus CCl_4 will add to olefines in presence of a peroxide,‡ although in its absence no reaction takes place. Alkyl radicals are known to abstract Cl from CCl_4 very easily, so the mechanism of the olefine addition is almost certainly

$$\left\{\begin{array}{l}(PhCOO)_2 \rightarrow 2Ph\cdot + 2CO_2 \\ Ph\cdot + CCl_4 \rightarrow PhCl + \cdot CCl_3\end{array}\right.$$



$$\left\{\begin{array}{l}\cdot CCl_3 + \overset{|}{\underset{|}{C}}{=}\overset{|}{\underset{|}{C}} \rightarrow Cl_3C{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}\cdot \\ Cl_3C{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}\cdot + CCl_4 \rightarrow Cl_3C{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}Cl + \cdot CCl_3, \text{ etc.}\end{array}\right.$$

Other compounds containing several chlorine atoms attached to one carbon add likewise to olefines (e.g. $CHCl_3$, $CHCl_2\cdot COOEt$).

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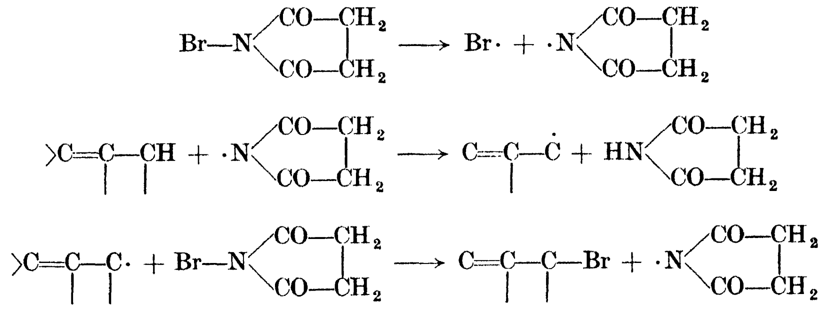
† See Steacie (p. 256).

‡ Kharasch, Elwood, Jensen, and Urry, *J.A.C.S.* 1947, **69**, 1100; Kharasch, Reinmuth, and Urry, ibid. p. 1105.

Bromination with N-bromoamides

It is now well established that olefines react with N-bromoamides to give allyl bromide derivatives, N-bromosuccinimide being the favourite reagent. Waters† found that cyclohexene could be chlorinated to 3-chlorocyclohexene by benzenediazonium chloride, and therefore suggested‡ that free halogen atoms are responsible for both reactions, since N—Br links are weak and benzenediazonium chloride is thought to decompose into Cl atoms in organic solvents (cf. p. 260). This mechanism seems certainly incorrect since it is known from the peroxide-catalysed and photochemical additions of halogen or HBr to olefines that halogen atoms attack the double bond rather than an α-CH. On the other hand, the mechanism probably does involve radical intermediates, and the reactions of N-bromosuccinimide with olefines are indeed catalysed by benzoyl peroxide.§ The most plausible explanation seems to be that radical chains are involved, and that these are started in the absence of a catalyst by fission of a small part of the bromoamide to radicals; i.e.



with the usual bimolecular termination reactions. The specific allylic bromination could then be ascribed to the low reactivity of the succinimidyl radical, which is mesomeric (the N radical centre conjugating with the two carbonyl groups). Addition of any radical to the C=C bond to give a simple alkyl radical should be energetically less favourable than removal of an α-hydrogen to give a mesomeric allyl radical; the difference between the reactions of active atoms or radicals, and of the relatively inactive succinimidyl radical, with olefines would then parallel the similar differences between the reactions of active and inactive ionic reagents with mesomeric ions (cf. p. 103). An interesting test would be provided by the bromination of higher olefines with terminal double bonds. Thus the olefine (II) should give an intermediate allyl radical (III), which should react with N-bromosuccinimide to form preferentially an ω-bromide (IV) (cf. p. 147).

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† *J.C.S.* 1939, 1805.

‡ *Nature*, 1944, **154**, 772.

§ Schmid and Karrer, *Helv. Chim. Acta*, 1946, **29**, 573. This does not prove that radicals are involved in the uncatalysed reaction, and it may possibly take place by an ionic mechanism. However, the N—Br bond is weak and it seems more likely that radicals are involved, particularly since the reactions take place readily in non-polar solvents, such as CCl_4.

$$\underset{\text{(II)}}{\mathrm{R{-}CH_2{-}CH{=}CH_2}} \qquad \underset{\text{(III)}}{\mathrm{R{-}CH\overset{\cdots}{-}CH\overset{\cdots}{-}CH_2}} \qquad \underset{\text{(IV)}}{\mathrm{R\cdot CH{=}CH\cdot CH_2Br}}$$

A possible example has been recently found by Karrer and Ringl;† diallyl (V) with two molecules of N-bromosuccinimide gives not 3:4-dibrom-1:5-hexadiene (VI), but 1:6-dibrom-2:4-hexadiene (VII). Since the reaction is carried out in a non-polar solvent, the product cannot be formed by anionotropic rearrangement of (VI). A monobromo derivative can be obtained from (V) by using less N-bromosuccinimide; its structure is still uncertain. The argument above would require it to be 1-bromo-2:5-hexadiene (VIII), bromination of which would naturally give the conjugated (VII). If the monobromo derivative actually has the structure (VIII), it will provide strong confirmation of the general mechanism, for the possibility of secondary rearrangement would be excluded (since it would certainly lead to a butadiene derivative).

$$\underset{\text{(V)}}{\mathrm{CH_2{=}CH\cdot CH_2\cdot CH_2\cdot CH{=}CH_2}} \qquad \underset{\text{(VI)}}{\mathrm{CH_2{=}CH\cdot CHBr\cdot CHBr\cdot CH{=}CH_2}}$$

$$\underset{\text{(VII)}}{\mathrm{BrCH_2{-}CH{=}CH{-}CH{=}CH{-}CH_2Br}} \qquad \underset{\text{(VIII)}}{\mathrm{CH_2{=}CH{-}CH_2{-}CH{=}CH{-}CH_2Br}}$$

Bromoamides will also attack other compounds which give stabilized radicals; for example, ketones, where the radical is stabilized by the $+E$ carbonyl, or tertiary C—H, since *tert*-alkyl radicals are known to be much more stable than primary or secondary alkyl (p. 262). These reactions take place much more easily in presence of peroxide catalysts.‡

Auto-oxidation

Many olefines will combine with molecular oxygen to form peroxides. These auto-oxidation reactions have been studied recently§ in some detail and their mechanism is now well established. Since they are catalysed by peroxides and strongly inhibited by standard inhibitors (e.g. quinone), a radical-chain mechanism is indicated. When ethyl linoleate (IX) is auto-oxidized,‖ the product contains a pair of conjugated double bonds, as is shown by its absorption spectrum. Hence one double bond at least must migrate during reaction. The kinetics are complicated by autocatalysis; the product of reaction is a peroxide, and can be shown by independent experiments to break down by a bimolecular reaction into radicals at appreciable speed under the conditions of the auto-oxidation. The radicals start new chains. Hence the rate of chain-starting increases steadily as the reaction proceeds. Gee and Bolland therefore suggested the following scheme (L represents a radical derived from ethyl linoleate by loss of one hydrogen atom).

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† *Helv. Chim. Acta*, 1947, **30**, 1771.

‡ Schmid and Karrer, ibid. 1946, **29**, 573.

§ See the Discussion on Oxidation, *Trans. Faraday Soc.* 1946, **42**, 99–396.

‖ Bolland, *Proc. Roy. Soc.* 1946, A **186**, 218; Bolland and Gee, *Trans. Faraday Soc.* 1946, **42**, 236, 244.

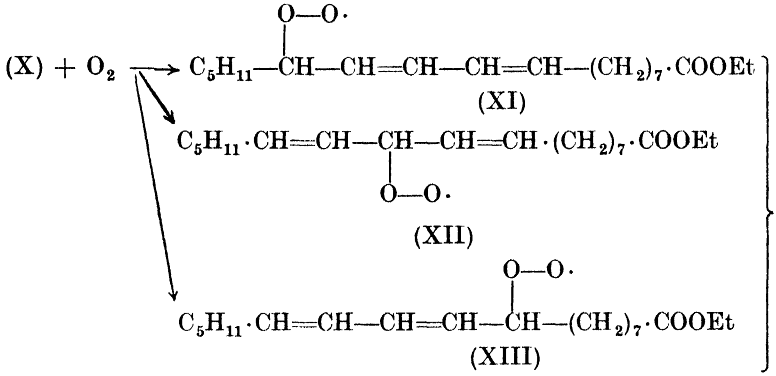
Initiation

$$2\text{L—O—OH} \rightarrow 2\text{LO}\cdot + 2\cdot\text{OH} \qquad (1)$$

$$\underset{\text{(IX)}}{\text{CH}_3(\text{CH}_2)_4\cdot\text{CH}{=}\text{CH}\cdot\text{CH}_2\cdot\text{CH}{=}\text{CH}\cdot(\text{CH}_2)_7\cdot\text{COOEt}} + \text{RO}\cdot$$

$$\rightarrow \underset{\text{(X)}}{\text{C}_5\text{H}_{11}\text{—CH}\cdots\text{CH}\cdots\text{CH}\cdots\text{CH}\cdots\text{CH}\cdot(\text{CH}_2)_7\cdot\text{COOEt}} + \text{ROH} \qquad (2)$$

Propagation



$$(\text{X}) + \text{O}_2 \rightarrow \underset{\text{(XI)}}{\text{C}_5\text{H}_{11}\text{—}\overset{\text{O—O}\cdot}{\text{CH}}\text{—CH}{=}\text{CH—CH}{=}\text{CH—}(\text{CH}_2)_7\cdot\text{COOEt}}$$

$$\rightarrow \underset{\text{(XII)}}{\text{C}_5\text{H}_{11}\cdot\text{CH}{=}\text{CH—}\underset{\text{O—O}\cdot}{\text{CH}}\text{—CH}{=}\text{CH}\cdot(\text{CH}_2)_7\cdot\text{COOEt}}$$

$$\rightarrow \underset{\text{(XIII)}}{\text{C}_5\text{H}_{11}\cdot\text{CH}{=}\text{CH—CH}{=}\text{CH—}\overset{\text{O—O}\cdot}{\text{CH}}\text{—}(\text{CH}_2)_7\cdot\text{COOEt}} \qquad (3)$$

$$\text{L—O—O}\cdot + (\text{IX}) \rightarrow \text{LOOH} + (\text{X}) \qquad (4)$$

Termination

$$2\text{L}\cdot \rightarrow \text{L}_2, \quad \text{etc.} \qquad (5)$$

$$\text{L}\cdot + \text{LOO}\cdot \rightarrow \text{L—O—O—L}, \quad \text{etc.} \qquad (6)$$

$$2\text{LOO}\cdot \rightarrow\ ? \qquad (7)$$

Radicals should easily remove an H atom from (IX) to give the mesomeric radical (X). This can combine with O_2 to form a peroxide radical in three different ways. Naturally terminal addition will predominate, the double bonds in (XI) and (XIII) being conjugated, those in (XII) unconjugated. Therefore the greater part of the resulting peroxide will contain conjugated double bonds. The formation and orientation of (XI) and (XIII) has been confirmed by hydrogenation of the resulting hydroperoxides to the corresponding hydroxystearic acids.†

It will be seen that the scheme for the auto-oxidation is formally identical with the general one on p. 268. The rate at which radicals are formed is $2k_1[\text{LOOH}]^2$. Therefore the overall rate of reaction, measured by the rate of oxygen uptake, is calculated to be

$$-\frac{d[\text{O}_2]}{dt} = \frac{k_3 k_4 \sqrt{(2k_1)}[\text{LOOH}][\text{LH}][\text{O}_2]}{k_3[\text{O}_2]\sqrt{k_7}+k_4[\text{LH}]\sqrt{k_5}}.$$

The observed rates agreed very closely with this expression.

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† Bergström and Theorell, ibid. 1946, **42**, 258.

The oxidations of other olefines were also studied and found to be similar in all important respects, so the same mechanism probably applies to other auto-oxidations.

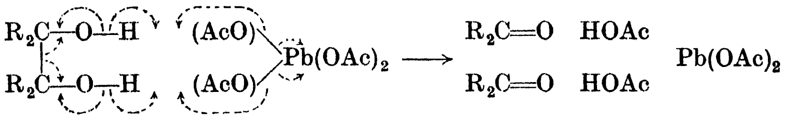
The Criegee and Malaprade reactions

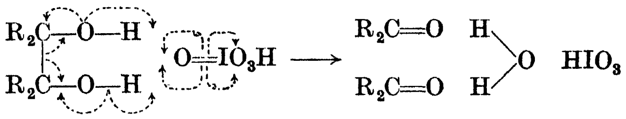
Lead tetraacetate and periodic acid have a specific action on 1:2-glycols and related compounds, oxidizing them to two molecules of carbonyl compounds, viz.

$$\begin{array}{l}R_2C\text{—}OH\\ \quad|\\ R_2C\text{—}OH\end{array} + Pb(OAc)_4 \longrightarrow \begin{array}{l}R_2C{=}O\\ \\ R_2C{=}O\end{array} + 2HOAc + Pb(OAc)_2$$

$$\begin{array}{l}R_2C\text{—}OH\\ \quad|\\ R_2C\text{—}OH\end{array} + HIO_4 \longrightarrow \begin{array}{l}R_2C{=}O\\ \\ R_2C{=}O\end{array} + H_2O + HIO_3$$

It is convenient to discuss these reactions at this point since they are not ionic, occurring equally readily in solvents of varying dielectric constant; and since Waters† has suggested that the Criegee reaction takes place by a radical mechanism, the lead tetraacetate splitting into $Pb(OAc)_2 + 2AcO\cdot$, and the acetate radicals then dehydrogenating the glycol. This interpretation seems hardly tenable since lead tetraacetate is stable under conditions where it oxidizes glycols rapidly and quantitatively. Moreover, if acetate radicals were intermediates, the stability of simple alcohols to the reagent would be inexplicable. It is much more likely that a bimolecular reaction between the reagent and the glycol is involved, not a preliminary unimolecular fission of the former. The mechanisms may be written





The essential feature of the two reagents is their ability to accept simultaneously the two H atoms from the glycol. The corresponding reaction with two molecules of an alcohol would give two radicals:

$$\begin{array}{l}R_3C\text{—}O\text{—}H\\ \\ R_3C\text{—}O\text{—}H\end{array} + Pb(OAc)_4 \longrightarrow \begin{array}{l}R_3C\text{—}O\cdot\\ \\ R_3C\text{—}O\cdot\end{array} + 2HOAc + Pb(OAc)_2.$$

From the bond-energy table it is easily seen that this reaction should be at least 100 Cals. less exothermic than the glycol oxidation, and so the failure of ordinary alcohols to react is not surprising. (In the oxidation of a glycol, free radicals are not formed, and so the reaction is more exothermic than the alcohol oxidation by the large energy of combination or disproportionation of the radicals.)

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† *The Chemistry of Free Radicals*, Clarendon Press, Oxford, 1946.

At high temperatures, lead tetraacetate does decompose appreciably to give free acetate radicals, and the Criegee reaction may give more complex products under such conditions. A reaction of this type is the direct introduction of acyloxy groups into molecules containing suitable +E substituents; for instance, acetic anhydride will give acetylglycollic anhydride, and toluene and many other alkylaromatic compounds give benzyl acetate or analogous products. The mechanism has commonly been thought to be

$$\mathrm{Pb(OAc)_4 \rightarrow Pb(OAc)_2 + 2AcO\cdot}$$
$$\mathrm{AcO\cdot + RCH_3 \rightarrow AcOH + RCH_2\cdot}$$
$$\mathrm{RCH_2\cdot + AcO\cdot \rightarrow R\cdot CH_2OAc}$$

It is, however, unlikely that the yields could be so high if this mechanism were correct since the concentration of radicals would have to be relatively large and by-products would be formed by decomposition of the acetate radicals (leading to methylation instead of acetoxylation) or by union of $\mathrm{R{-}CH_2\cdot}$ radicals in pairs. Moreover, lead tetraacetate seems to decompose more rapidly in presence of compounds which can give mesomeric radicals (and can therefore react readily with radicals). It is quite likely that a radical-chain mechanism operates:

$$\begin{array}{ll} \text{Initiation} & \mathrm{Pb(OAc)_4 \rightarrow Pb(OAc)_2 + 2AcO\cdot} \\ \text{Propagation} & \left\{\begin{array}{l} \mathrm{AcO\cdot + RCH_3 \rightarrow AcOH + RCH_2\cdot} \\ \mathrm{RCH_2\cdot + Pb(OAc)_4 \rightarrow R\cdot CH_2OAc + Pb(OAc)_2 + AcO\cdot} \end{array}\right. \\ \text{Termination} & \mathrm{AcO\cdot + R\cdot \rightarrow ROAc} \end{array}$$

In this case only one termination reaction should occur readily; the radicals $\mathrm{RCH_2\cdot}$ are mesomeric and hence their bimolecular union will be relatively slow, while dimerization of acetoxyl would give a peroxide which under the conditions of reaction would readily dissociate, regenerating acetoxyl radicals.

Oxidation with Fenton's reagent does, however, take place by direct radical attack. The ferrous ion decomposes the hydrogen peroxide into $\mathrm{HO\cdot}$ radicals which are the active oxidants.†

$$\mathrm{H_2O_2 + Fe^{++} \rightarrow HO\cdot + H\bar{O} + Fe^{+++}}$$

The $\mathrm{Fe^{++}}$ ion acts as a one-electron donor and hence reacts with $\mathrm{H_2O_2}$ to give an $\mathrm{\bar{OH}}$ ion and an $\mathrm{OH\cdot}$ radical. The reagent seems to act essentially as a hydroxylating agent,

$$\mathrm{RH + OH\cdot \rightarrow R\cdot + HOH}$$
$$\mathrm{R\cdot + \cdot OH \rightarrow ROH.}$$

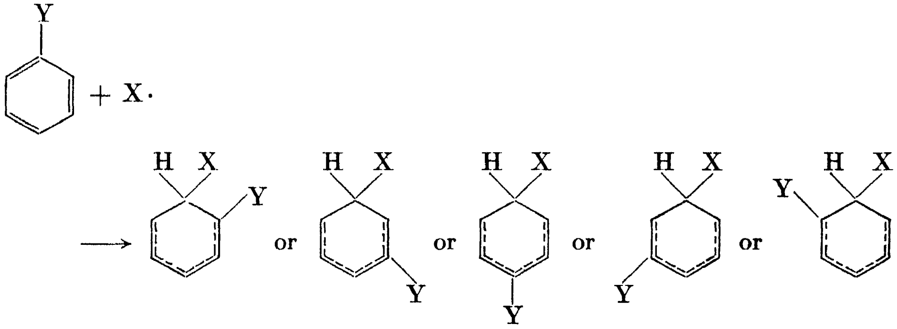
---

† Haber and Weiss, *Proc. Roy. Soc.* 1939, A **147**, 332.

It is interesting that tartaric acid is oxidized to dioxymaleic acid by the reagent and not to glyoxylic acid; $Pb(OAc)_4$ gives ethyl glyoxylate with ethyl tartrate, and HIO_4 oxidizes the acid or ester to glyoxylic acid derivatives. This result again indicates that free radicals are not intermediates in the Criegee or Malaprade reactions.

Aromatic substitution by radicals

Besides anionoid and cationoid substitution, a third process is possible where the reagents are free radicals and displace atoms or radicals from aromatic systems. The best known examples are the arylations of aromatic rings by free aryl radicals prepared by decomposition of diazohydroxides or nitrosoamides, but other radicals or atoms react likewise. The most striking feature of these reactions is the ease with which they occur, and the orientation of the products; a monosubstituted benzene always gives mainly *o*- or *p*-disubstituted benzenes by reaction with radicals, no matter what the first substituent may be. The reason for this is very simple. The transition states for the substitution may be formally written,

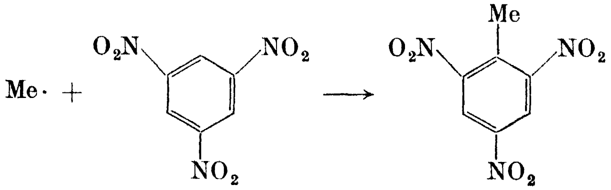


(*a*) (*b*) (*c*) (*d*) (*e*)

each containing a pentadienyl radical (cf. p. 163). The pentadienyl radical may in theory be derived from a normal pentadienyl anion by loss of one electron, or from a normal pentadienyl cation by gain of one electron. The arguments on p. 243 then lead us to suppose that any substituent which stabilizes either of the parent ions will stabilize the radical, although substituents stabilizing the anion will be the more effective. Therefore any substituent will stabilize the radical, but positive substituents will be more active than negative, and all substituents will be more active in the 1-, 3-, or 5-positions in the radical. Hence all substituents should accelerate radical substitution of benzene, especially in the *o*–*p*-positions, and positive substituents should be more active than negative. It is indeed found that arylation of benzene by aryl radicals is facilitated by any substituent in the benzene, but that positive substituents are much the most effective, nitrobenzene arylating with exceptional ease.

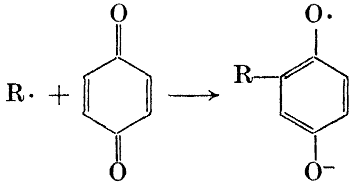
Alkyl radicals, being less active than aryl, cannot as a rule substitute aromatic nuclei, but if the nucleus is activated by sufficient positive substituents such reactions can occur. Thus trinitrobenzene gives trinitrotoluene and trinitro-*m*-xylene with hot lead tetraacetate or acetyl peroxide,† reactions which very probably take place through the intermediate production of acetate radicals and their decomposition to free methyl and CO_2. The detailed mechanism is, however, uncertain and may involve radical chains. We may write it formally as

$$\mathrm{Pb(OAc)_4} \rightarrow \mathrm{Pb(OAc)_2} + 2\mathrm{AcO}\cdot$$
$$\mathrm{AcO}\cdot \rightarrow \mathrm{Me}\cdot + \mathrm{CO_2}$$



The fate of the hydrogen theoretically formed in these reactions is uncertain; it may reduce part of the reactants, or initiate the decomposition of more of the radical-forming material. In the alkylation of nitro-compounds the yields are generally very poor and so no conclusions can be drawn on this point. It is interesting that quinone, another strongly cationoid system, also reacts very easily with alkyl radicals formed from acyl peroxides, giving alkylquinones; the mechanism is probably

$$\mathrm{(RCOO)_2} \rightarrow \mathrm{R}\cdot + \mathrm{CO_2}$$



The product is then a radical, electronically analogous to a Würster salt. The great ease of reaction of polynitro compounds and quinones with radicals, and the stability of the products, makes these compounds exceptionally good inhibitors of radical-chain reactions.

Two further cases of radical substitution may be mentioned. Pyridine gives a mixture of all three phenylpyridines with free phenyl radicals, the α and γ isomers predominating; this result follows from the electronic analogy of pyridine to nitrobenzene. And secondly, both pyridine and bromobenzene give abnormal products on bromination at high temperatures (425–450°) in the absence of catalysts, both giving mixtures of all the possible isomers in comparable amounts. Since normal orientation is observed at slightly lower temperatures or in presence of cationoid catalysts, it seems likely‡ that the abnormal products are formed by the direct action of bromine atoms derived from the thermal dissociation of Br_2 at the temperatures used.

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† Fieser, Clapp, and Daudt, *J.A.C.S.* 1942, **67**, 2043, 2053.

‡ Waters, *Trans. Faraday Soc.* 1941, **37**, 745.

Conclusion

The general theory of radical reactions is still in a very unsatisfactory state. A number of simple processes involving radicals have been studied in the gas phase,† but the conclusions drawn from them have little direct application to reactions in solution. The gas phase reactions generally deal with only the simplest radicals whose reactions often differ from the more complex ones commonly met in organic chemistry. The measurement of rates of individual radical reactions in solution is one of the most pressing unsolved problems of chemical kinetics, for without it no really satisfactory theory of the relation between structure and rate can be built up (cf. p. 290).

† A detailed discussion has been given by Steacie (op. cit., p. 256). Gas reactions have not been discussed here since an adequate treatment would not be possible without disproportionate expenditure of space; and since they do not introduce any new principles into the general electronic theory.

CHAPTER XIV

POLYMERIZATION

IT has long been known that many substituted ethylenes readily polymerize, but the mechanism of the polymerizations has only recently been established. The physical properties of the polymers show that their molecules are linear, and general principles suggest that they are formed by end-to-end union of the C═C units:

$$\mathrm{C{=}C\quad C{=}C\quad C{=}C,\ etc}$$
$$\rightarrow \mathrm{-C-C-C-C-C-C-,\ etc}$$

Such a reaction should be exothermic, the polymer containing two C—C single bonds in place of each C═C bond in the monomer: the heat of polymerization deduced from the bond-energy table is then 18 Cals./Mol. of monomer, and the observed[†] heats of polymerization are roughly equal to this. In some cases the linear backbone of the polymer may be branched to some extent.

The polymerizations are of five main types. In the first three, reaction takes place under the influence of active 'catalysts', anionoid, cationoid, or radical reagents. Their action is not truly catalytic, a molecule of catalyst invariably being incorporated into the polymer, but since the molecular weight of the latter may be a million or more, the quantity of catalyst incorporated into the polymer may be extremely small. Polymerization may also be initiated by light, and in some cases vinyl compounds polymerize spontaneously.

The formation of a polymer molecule seems to be an extremely rapid process. If the polymer grew slowly by successive additions of monomer, the molecular weight would increase gradually with time. This is the case in polycondensation reactions, for instance, the polyesterification of hydroxy acids.[‡] In vinyl polymerizations, however, the molecular weight usually remains more or less constant throughout the reaction; the actual formation of a polymer molecule must occupy a very short space of time, and the 'dead polymer' that results plays no further part in the reaction. The only reasonable interpretation, and it is in full accord with all the known facts, is that polymerization is a chain reaction in which the product really *is* a chain. Some process activates a molecule of monomer; this adds a second monomer molecule to give an active dimer, which in turn adds a third monomer molecule to give an active trimer, and so forth. Eventually the active centre is deactivated in some way leaving a 'dead' polymer molecule. The growth, or propagation phase is extremely rapid compared with the overall rate at which monomer is converted into polymer. The active centre can only be a positive or negative carbonium ion or a radical. These ionic polymerizations are the only ionic chain reactions known.

[†] Cf. Tong and Kenyon, *J.A.C.S.* 1945, **67**, 1278; 1946, **68**, 1335; 1947, **69**, 1402, 2245.

[‡] For a survey see Carrothers, *High Polymers*, **1**, Interscience Publishers, 1939.

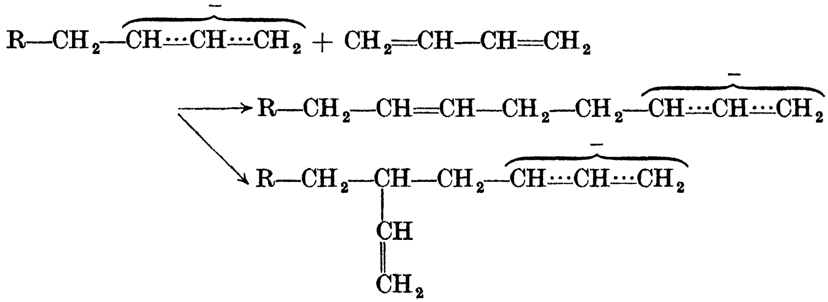
Anionoid polymerization

Butadiene is catalytically polymerized by alkali metals or by alkali metal alkyls. The mechanism of this reaction, which is used in Russia to make synthetic rubber, has been established by Ziegler and his collaborators.† Normally the reactions are too fast for study, but by choosing catalysts of low activity (lithium alkyls) and diluting the butadiene with ether, Ziegler was able to isolate the lower polymers, dimer, trimer, etc., and to show that the alkyl from the catalyst was incorporated into the polymer. He also showed that lithium metal would add to butadiene to give a dilithium derivative, $Li{-}CH_2{-}CH{=}CH{-}CH_2{-}Li$, which then added butadiene at each end. And finally the rapid reactions with sodium were shown to have a similar mechanism by carrying them out in presence of compounds (especially secondary aliphatic amines) which react with sodium alkyl but not with sodium. Again dimer, trimer, etc., could be isolated in which the intermediate ions had reacted with the 'retarder' to give hydrocarbons and a relatively inert anion derived from the retarder (e.g. R_2N^-).

The general mechanism of the reaction is thus clear. The catalyst is either an active anion or a metal which reacts with butadiene to give a negative ion. The ion adds to butadiene to form a substituted allyl anion:

$$R^- + CH_2{=}CH{-}CH{=}CH_2 \rightarrow R\cdot CH_2{-}\overset{-}{\overparen{CH\cdots CH\cdots CH_2}}$$

This anion can add a second butadiene molecule in two ways:



$$\begin{array}{l} R{-}CH_2{-}\overset{-}{\overparen{CH\cdots CH\cdots CH_2}} + CH_2{=}CH{-}CH{=}CH_2 \\ \quad\rightarrow R{-}CH_2{-}CH{=}CH{-}CH_2{-}CH_2{-}\overset{-}{\overparen{CH\cdots CH\cdots CH_2}} \\ \quad\searrow R{-}CH_2{-}\underset{\underset{\displaystyle CH_2}{\|}}{\underset{\displaystyle CH}{\underset{|}{CH}}}{-}CH_2{-}\overset{-}{\overparen{CH\cdots CH\cdots CH_2}} \end{array}$$

The reaction resembles, with charges reversed, cationoid addition to butadiene (p. 147); similar arguments might suggest that 1:4 addition should be energetically favoured. Ziegler‡ has, however, found that 1:2 addition predominates at low temperatures, 1:4 at high temperatures, in the anionoid polymerization. This must imply (p. 174) that 1:4 polymerization has the *higher* activation energy, but also the higher frequency factor. The explanation seems to be this. The allyl anion, a —E group, cannot hyperconjugate with $-E$ alkyl groups. Therefore in the ion $RCH_2\text{—}\overbrace{CH\cdots CH\cdots CH_2}^{-}$, the RCH_2 can only exercise its $-I$ effect, reducing the electron affinity of the adjacent allylic carbon. The mesomeric system then approximates to that of an enolate ion, the terminal methylene in the former, and the oxygen in the latter, having relatively high electron affinities. The orientation of addition is therefore similar in both cases (see p. 103). In anionoid addition to an allyl cation,

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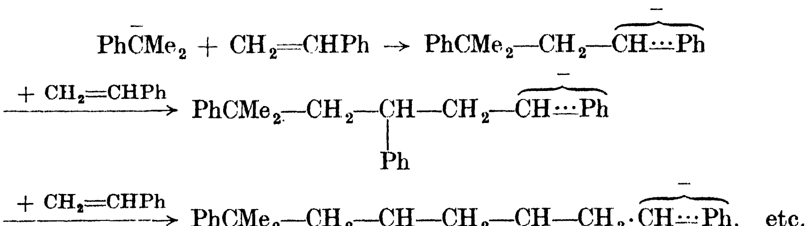
† *Ber.* 1928, **61**, 253; *Annalen*, 1929, **473**, 1; 1934, **511**, 13, 45, 64.

‡ Ibid. 1938, **542**, 90.

$$RCH_2\text{—}\overbrace{CH\cdots CH\cdots CH_2}^{+},$$

the RCH_2 can hyperconjugate with the $+E$ allyl system and the orientation is therefore different.

Simple olefines do not show any cationoid reactivity (p. 142) and therefore do not polymerize on treatment with metals or active anions. The reactivity of butadiene may be ascribed to the large resonance energy of the allyl anion which greatly facilitates addition of anions to the diene. The addition must of course occur at the terminal carbon for this to be so; Ziegler has shown that the anion does add terminally. It should be possible for other $+E$-substituted ethylenes to be polymerized by active ions. Little work has been done in this connexion, but styrene is readily polymerized by alkali metals or by phenyl*iso*propyl potassium; the intermediates are mesomeric benzyl anions, provided that polymerization always takes place by 'head-to-tail' addition of monomer.



$$Ph\bar{C}Me_2 + CH_2{=}CHPh \rightarrow PhCMe_2\text{—}CH_2\text{—}\overbrace{CH\cdots Ph}^{-}$$

$$\xrightarrow{+\,CH_2=CHPh} PhCMe_2\text{—}CH_2\text{—}\underset{\substack{|\\ Ph}}{CH}\text{—}CH_2\text{—}\overbrace{CH\cdots Ph}^{-}$$

$$\xrightarrow{+\,CH_2=CHPh} PhCMe_2\text{—}CH_2\text{—}\underset{\substack{|\\ Ph}}{CH}\text{—}CH_2\text{—}\underset{\substack{|\\ Ph}}{CH}\text{—}CH_2\cdot\overbrace{CH\cdots Ph}^{-},\quad \text{etc.}$$

The polymerization with sodium metal is interesting; following Ziegler's technique, Midgley, Henne, and Leicester[†] carried out the reaction in presence of alcohol and isolated ethylbenzene and 1:4-diphenylbutane. The most likely mechanism involves a preliminary transfer of an electron from the metal to styrene to give an ion-radical which then reacts as follows:

$$Na\cdot + Ph\cdot CH{=}CH_2 \rightarrow \overset{+}{Na}\ \overbrace{Ph\cdots CH}^{-}\text{—}CH_2\cdot$$

$$\overbrace{PhCH}^{-}\text{—}CH_2\cdot + EtOH \rightarrow EtO^- + Ph\cdot CH_2\cdot CH_2\cdot$$

$$Na\cdot + PhCH_2CH_2\cdot \rightarrow PhCH_2\cdot CH_2^- + Na^+$$

$$PhCH_2\cdot CH_2^- + EtOH \rightarrow Ph\cdot CH_2\cdot CH_3 + EtO^-$$

[†] *J.A.C.S.* 1936, 58, 1961.

$$\overbrace{2\,\overset{-}{\text{PhCH}}}\text{—CH}_2\cdot \rightarrow \overbrace{\overset{-}{\text{PhCH}}}\text{—CH}_2\text{—CH}_2\text{—}\overbrace{\overset{-}{\text{CHPh}}}$$

$$\xrightarrow{2\,\text{EtOH}} \text{Ph}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{Ph} + 2\text{EtO}^-$$

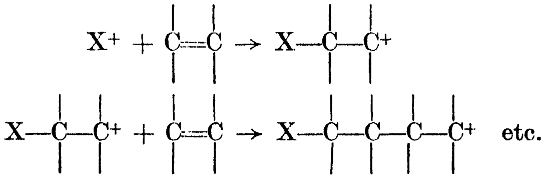
It is interesting that *as*-diphenylethylene does not polymerize with sodium, but gives a disodio derivative of 1:1:4:4-tetraphenylbutane:

$$2\text{Na} + 2\text{Ph}_2\text{C{=}CH}_2 \rightarrow \overset{\text{Na}^+}{\text{Ph}_2\overset{-}{\text{C}}}\text{—CH}_2\cdot\text{CH}_2\text{—}\overset{\text{Na}^+}{\overset{-}{\text{C}}\text{Ph}_2}$$

The reactivity of the resulting dianion is apparently too small for condensation with more monomer to occur; benzhydryl anions are of course more stable, and so less reactive, than benzyl anions.

Cationoid polymerization

Olefines are also polymerized by powerful cationoid reagents such as BF_3, $SbCl_5$, $AlCl_3$, or strong acids which act as sources of H^+. Now in presence of such reagents olefines can alkylate aromatic compounds, undoubtedly by the intermediate formation of carbonium ions, and addition of hydrogen halides by the ionic mechanism also involves carbonium ion intermediates (we shall ignore the possibility that the 'carbonium ions' may be π-complexes since it is irrelevant to the present argument). It therefore seems likely that carbonium ions can add to the double bonds of olefines to give larger carbonium ions. The mechanism of the polymerization will then be (X^+ being the cationoid catalyst),



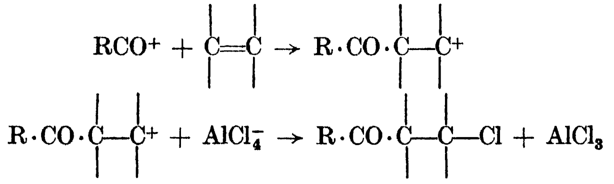
$$X^+ + \text{C{=}C} \rightarrow \text{X—C—C}^+$$

$$\text{X—C—C}^+ + \text{C{=}C} \rightarrow \text{X—C—C—C—C}^+ \quad \text{etc.}$$

This mechanism is supported by several lines of evidence.

Firstly, olefines react with acyl chlorides in presence of aluminium chloride to form chloroalkyl ketones, undoubtedly by the mechanism

$$\text{R}\cdot\text{CO}\cdot\text{Cl} + \text{AlCl}_3 \rightarrow \text{RCO}^+ \quad \text{AlCl}_4^-$$

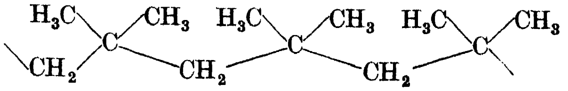


$$\text{RCO}^+ + \text{C{=}C} \rightarrow \text{R}\cdot\text{CO}\cdot\text{C—C}^+$$

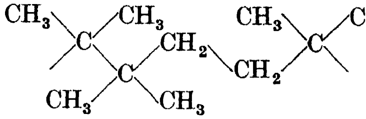
$$\text{R}\cdot\text{CO}\cdot\text{C—C}^+ + \text{AlCl}_4^- \rightarrow \text{R}\cdot\text{CO}\cdot\text{C—C—Cl} + \text{AlCl}_3$$

Hence acyl cations can almost certainly add to olefines and by inference alkyl cations should react likewise.

Secondly, the orientation of addition to unsymmetrical olefines should follow the same principles as other olefine additions. Addition should take place in such a way that the more stable cation is formed. Thus polymerization should occur by 'head-to-tail' addition of olefine molecules. Now in the case of *iso*-butene the head-to-tail polymer (I) is seen from models to be sterically hindered and strained, the head-to-head, tail-to-tail polymer (II) unstrained.



(I)



(II)

The heat of polymerization of *iso*-butene catalysed by BF_3 is considerably lower than those of olefines which can give unhindered polymers;† hence it seems very likely that poly*iso*butene has the head-to-tail orientation that theory requires, in spite of its unfavourable stereochemistry.

And thirdly, the molecular weights of polystyrenes, prepared by the catalytic action of metal chlorides, differ little when the rate of polymerization is varied greatly. Now the molecular weight of a polymer depends on the ratio of the rates at which the intermediate cations add monomer or are converted to inactive products. Since styrene gives stable molecules by Friedel–Craft reaction with acyl cations, it is likely that a similar reaction with the postulated cationic intermediates would give inert products, and so act as a molecule-ending mechanism. The rate of propagation will be given by

$$k_1[X][S],$$

where [X] is the concentration of intermediate cations, [S] of styrene; while the rate of Friedel–Craft termination will be

$$k_2[X][S].$$

The degree of polymerization (i.e. the number of monomer units per polymer chain) will then be given by

$$\bar{P} = \frac{k_1[X][S]}{k_2[X][S]} = \frac{k_1}{k_2}$$

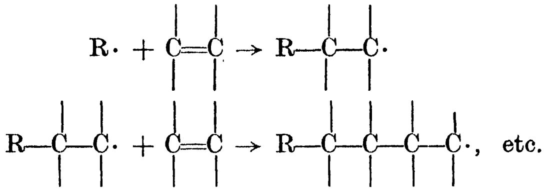
being therefore independent of the concentration of X and hence of the rate of polymerization. The polymerization of *iso*-butene must follow a different course since *iso*-butene does not undergo Friedel–Craft substitution reactions with alkyl cations; the degree of polymerization of *iso*-butene varies greatly with the conditions of reaction.

The ease of cationoid polymerization will run parallel to the ease of olefinic addition reactions, being increased by negative, decreased by positive substituents. Little is known of their effects, but styrene is polymerized almost explosively by cationoid reagents which have little effect on methyl methacrylate.

† Brown and Barbaras, *J. Chem. Phys.* 1946, **14**, 114.

Radical polymerizations

Radicals catalyse the polymerization of olefines; by analogy with ionic polymerization and with typical addition reactions of olefines with radicals, we may postulate the mechanism



$$\mathrm{R\cdot + C{=}C \rightarrow R{-}C{-}C\cdot}$$
$$\mathrm{R{-}C{-}C\cdot + C{=}C \rightarrow R{-}C{-}C{-}C{-}C\cdot}, \quad \text{etc.}$$

This mechanism is supported by three lines of evidence. Firstly, the reactions are strongly inhibited by quinones and other compounds that are known to react readily with radicals. Moreover, when nitro-compounds are used as inhibitors, molecules of inhibitor are incorporated into the polymers formed.† Secondly, substances known to form radicals easily, peroxides, diazohydroxides, N-nitrosoacylanilides, etc., are powerful polymerization catalysts, and when halobenzoyl peroxides are used as catalysts the polymers so formed contain halogen.‡ There is therefore clear evidence that radicals can start polymerizations, and that radical inhibitors can then remove the polymerization intermediates. Thirdly, the kinetics of these polymerizations can be well interpreted in terms of radical intermediates, as will be seen presently.

Photochemical polymerization

Many olefines are polymerized by ultra-violet light. It seems extremely likely that the reactions involve radicals, since photochemical reactions nearly always involve radical intermediates. Moreover, photochemical polymerizations are inhibited by quinones and other typical radical inhibitors, and their kinetics show that they resemble the radical-catalysed reactions.

Thermal polymerization

Many olefines polymerize spontaneously. These reactions also seem to take place by radical mechanisms since they are inhibited by radical inhibitors and, moreover, they take place in solution in phenols§ which would at once react with either positive or negative carbonium ions.

Kinetics of radical polymerization

Polymerization is apparently a more complex process than other radical-chain reactions because the intermediates are not all the same. There is no proof that the intermediate radicals all react at the same rate with monomer or with each other. However, it is reasonable to assume that the radicals are all equally reactive since it can make little difference to the radical centre whether it is at the end of a chain of ten or ten thousand monomer units. The general scheme, once more assuming bimolecular termination, may then be written

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† Price and Read, *J. Polymer Research*, **1946**, **1**, 46.

‡ Cf. Price and Tate, *J.A.C.S.* 1943, **65**, 517.

§ Walling, ibid. 1944, **66**, 1602.

$$? \rightarrow \mathrm{X} \tag{1}$$

$$\mathrm{X} + \mathrm{M} \rightarrow \mathrm{X} \tag{2}$$

$$2\mathrm{X} \rightarrow 2\mathrm{P}, \tag{4}$$

where X is the intermediate growing polymer radical, M the monomer, and P the dead polymer. Applying the stationary state method,

$$\frac{d[\mathrm{X}]}{dt} = k_1 - k_4[\mathrm{X}]^2 = 0,$$

hence $$[\mathrm{X}] = \sqrt{\frac{k_1}{k_4}}.$$

The overall rate of polymerization, i.e. the rate of disappearance of monomer, is given by

$$-\frac{d[\mathrm{M}]}{dt} = k_2[\mathrm{M}][\mathrm{X}] = k_2[\mathrm{M}]\sqrt{\frac{k_1}{k_4}}.$$

Hence the overall rate should be proportional to the square root of the rate of chain starting. In the catalysed reaction the rate should be proportional to the square root of catalyst concentration; in the photochemical reaction to the square root of the light absorbed. Both these relations are found to hold.

If the thermal polymerization were of the same type, and the starting reaction were

$$a\mathrm{M} \rightarrow \mathrm{X},$$

the rate of the starting reaction would be

$$k[\mathrm{M}]^a.$$

Hence the overall rate would be

$$-\frac{d[\mathrm{M}]}{dt} = k_2[\mathrm{M}]\sqrt{\left(\frac{k[\mathrm{M}]^a}{k_4}\right)}$$

$$= k_2\sqrt{\frac{k}{k_4}}.[\mathrm{M}]^{(1+\frac{1}{2}a)}.$$

From experiments with solutions in inert solvents, the thermal polymerization of styrene is found to be of the second order with respect to monomer; hence $1+\frac{1}{2}a = 2$ or $a = 2$. The chain-starting reaction is therefore a bimolecular reaction of the monomer. This result is not surprising. The initiation process involves the conversion of one or more normal monomer molecules into a diradical. From the bond-energy table we may deduce

$$\mathrm{C{=}C} \rightarrow \cdot\mathrm{C{-}C}\cdot \quad -63\cdot5 \text{ Cals.},$$

$$\mathrm{C{=}C} + \mathrm{C{=}C} \rightarrow \cdot\mathrm{C{-}C{-}C{-}C}\cdot \quad -46 \text{ Cals.}$$

Hence the bimolecular reaction is energetically more favourable than the unimolecular. Naturally the energy required will be less if the resulting diradical is mesomeric, and, indeed, spontaneous polymerization never occurs at all readily unless such is the case.

Molecular weights ; the transfer reaction

The mean degree of polymerization, that is, the average number of monomer units in each polymer molecule, will be equal to the ratio of propagation rate to termination rate; for this ratio measures the number of times propagation takes place on average before a radical centre terminates. In the above scheme we then have

$$\bar{P} = \frac{k_2[\mathrm{X}][\mathrm{M}]}{k_4[\mathrm{X}]^2} = \frac{k_2[\mathrm{M}]}{\sqrt{(k_1 k_4)}},$$

and hence $\bar{P}$ should be inversely proportional to the square root of the rate of chain starting. This relation has been observed by many authors in catalysed polymerizations of pure monomers, where the mean degree of polymerization is inversely proportional to the square root of the catalyst concentration.

When polymerization is carried out in a solvent, the molecular weight of the polymer is generally less than that of the polymer prepared from pure monomer under similar conditions. The overall rate of polymerization still obeys the law derived above. The only reasonable explanation seems to be that a growing polymer radical can react with a solvent molecule to give a dead polymer and a new radical. The new radical starts a new chain. This *transfer reaction*† does not alter the effective concentration of radicals in the solution, and hence the rate of removal of monomer is unaffected; but it does chop up each polymer molecule into smaller units. Thus if $\bar{P}$ would in the absence of transfer be 10^4, and if transfer occurs ten times more rapidly than bimolecular termination, the original polymer molecule will on average be replaced by ten molecules each with $\bar{P} = 10^3$. As Flory† remarked, similar transfer should also occur with pure monomer. The transfer reaction with a simple molecule T may be written

$$\mathrm{X}+\mathrm{T} \rightarrow \mathrm{P}+\mathrm{X}; \tag{3}$$

combining this with the equation previously given we have

$$\bar{P} = \frac{k_2[\mathrm{M}]}{k_3[\mathrm{T}]+\sqrt{(k_1 k_4)}}, \tag{4}$$

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† Flory, *J.A.C.S.* 1937, **59**, 241.

whence
$$\frac{1}{\bar{P}} = \frac{1}{\bar{P}_0} + \frac{k_3}{k_2} \cdot \frac{[\mathrm{T}]}{[\mathrm{M}]}, \tag{5}$$

where $\bar{P}$ is the mean degree of polymerization of the solvent polymer, $\bar{P}_0$ that of polymer prepared in absence of solvent.

Mayo[†] has shown that the observed variation of $\bar{P}$ with monomer concentration obeys this law for the polymerization of styrene in a number of solvents.

Nature of the transfer reaction

When styrene is polymerized in carbon tetrachloride solution, low polymers are formed which contain chlorine. The reduction of molecular weight is, as we have seen, due to a chain transfer reaction with the solvent; and it appears that transfer somehow leads to an incorporation of solvent into the polymer molecules.

Now carbon tetrachloride is known to react readily with an alkyl radical to form an alkyl chloride and a $\cdot CCl_3$ radical. The most natural explanation of the transfer reaction would then seem to be that the growing polymer radical abstracts chlorine from the solvent to give a dead chlorine-containing polymer and a $\cdot CCl_3$ radical which can react with more styrene to start a new chain. The whole process is thus precisely analogous to the peroxide-catalysed addition of carbon tetrachloride to olefines (p. 272), except that in the polymerization the intermediate alkyl radicals first add a number of monomer molecules before reacting with the carbon tetrachloride, thus:

Simple addition

$$Cl_3C\cdot + C{=}C \rightarrow Cl_3C{-}C{-}C\cdot$$
$$Cl_3C{-}C{-}C\cdot + CCl_4 \rightarrow Cl_3C{-}C{-}C{-}Cl + Cl_3C\cdot$$

Polymerization with transfer

$$Cl_3C\cdot + C{=}C \rightarrow Cl_3C{-}C{-}C\cdot$$
$$Cl_3C{-}C{-}C\cdot + C{=}C \rightarrow Cl_3C{-}C{-}C{-}C{-}C\cdot, \text{ etc.}$$
$$Cl_3C{-}(C{-}C)_n{-}C{-}C\cdot + CCl_4 \rightarrow Cl_3C(C{-}C)_{n+1}\cdot Cl + Cl_3C\cdot$$

There can be little doubt that chain transfer always takes place by the same general mechanism. In every case that has been investigated a similar incorporation of solvent into the polymer has been observed.[‡] A particularly striking confirmation has been found recently. Kharasch and his collaborators had shown (cf. p. 272) that excess carbon tetrabromide will react with styrene in presence of peroxide catalysts to give an almost quantitative yield of the tetrabromopropane derivative (III). It has now been found[§] that the thermal polymerization of styrene containing small amounts of carbon tetrabromide gives bromine-containing polymers which undoubtedly have the structure (IV), and whose molecular weights follow equation (5). The only reasonable explanation would seem to be that both reactions have the same general mechanism, the product (III) being a 'polymer' with P = 0 obtained in quantity when k_3[T] in equation (5) is sufficiently large.

[†] Mayo, ibid. 1943, **65**, 2324; Gregg and Mayo, *Faraday Society Discussion on the Labile Molecule*, 1947, and *J.A.C.S.* 1948; cf. Bamford and Dewar, ibid., and *Proc. Roy. Soc.* 1948, A **192**, 329.

[‡] Cf., for example, Price and Read, *J. Polymer Science*, 1946, **1**, 44.

[§] Bamford and Dewar, loc. cit. and p. 290.

$Ph{\cdot}CHBr{\cdot}CH_2{\cdot}CBr_3$ (III) $Ph{\cdot}CHBr{\cdot}CH_2(PhCH{\cdot}CH_2)_n{\cdot}CBr_3$ (IV)

Two further points arise. Firstly, a chain transfer reaction with the monomer itself should be possible. Substituting [M] for [T] in equation (4) we should then expect $\bar{P}$ to be given by

$$\bar{P} = \frac{k_2[M]}{k_3[M]+\surd(k_1 k_4)}. \tag{6}$$

A relation of this type has indeed been shown to hold in the polymerizations of styrene and methyl methacrylate.† It is easily seen that this additional transfer reaction does not alter equation (5) for solvent polymerization.

Secondly, the chain-transfer reaction differs from the reaction of a polymer radical with an inhibitor only in that in the latter case the transfer radical is too inert to start a new polymer chain. An interesting corollary follows; suitable structural modification of an inhibitor may so increase the reactivity of the radicals formed by transfer that it may cease to be an inhibitor at all and become a chain-transfer agent. Thus quinone is an extremely powerful inhibitor, while chloranil has no appreciable inhibiting action on the polymerization of styrene, although it does by chain transfer reduce the molecular weight of the product.‡

The quantitative study of radical reactions

A comparison of the kinetic scheme for polymerization with that given for general radical chain reactions in the last chapter shows that the former is very much the simpler. Polymerization of a pure monomer involves only four distinct processes, initiation, propagation, transfer, and termination, while the other chain reactions involve two separate propagation reactions and three terminations. The study of polymerization therefore provides the most hopeful approach to a quantitative study of the rates of radical reactions, which is essential for any further development of electronic theory in that direction. At present three profitable lines of approach are being pursued.

1. Swain and Bartlett,§ Burnett and Melville,|| and Bamford and Dewar†† have described three methods for determining the velocity constants in

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† Bamford and Dewar, loc. cit. (p. 289) and *Proc. Roy. Soc.* 1948, A **192,** 309. These authors give a more complete and elaborate kinetic analysis which, however, involves no new principles.

‡ Price, *J.A.C.S.* 1943, **65,** 2380; Breitenbach and Taglieber, *Ber.* 1943, **76,** 272.

§ *J.A.C.S.* 1946, **68,** 2381.

|| *Proc. Roy. Soc.* 1947.

†† See ref. † above, and † on p. 291.

vinyl polymerizations absolutely. Of these the method of Burnett and Melville is open to criticism,† but by the other methods all the velocity constants have been determined for vinyl acetate, styrene, and methyl methacrylate. Extension of these measurements to other monomers will provide much useful information.

2. Mayo (see p. 289) has compared the rates of chain transfer of polystyryl radicals with solvents. When his method is supplemented with the absolute velocity constants which are now available, the absolute rates of the transfer reactions can be found. The rate of reaction can then be correlated with solvent structure. The transfer reaction is essentially a radical replacement:

$$R\cdot + X—Y \rightarrow R—X + Y\cdot$$

It should be facilitated by an increase in the R—X bond-energy, a decrease in the X—Y bond-energy, an increase in resonance energy of the radical Y, or a decrease in resonance energy of the radical R·. Therefore if we confine attention to a series of transfer reactions for the same monomer in different solvents, the rate should increase with decreasing bond-energy of the solvent bond which is split in the transfer reaction, and with increasing resonance energy of the resulting radical. These relations seem to hold; thus alkyl halides react more readily than do corresponding hydrocarbons, and in the order $RI > RBr > RCl$; in these reactions polymer radicals abstract hydrogen or halogen from the solvent; and the bond-energies fall in the series $C—H > C—Cl > C—Br > C—I$. Moreover, toluene, which can give a mesomeric benzyl radical, reacts more readily than does benzene or a paraffin, and diphenylmethane and triphenylmethane react more readily still; while carbon tetrahalides, which can give mesomeric radicals $X_3C\cdot$, react more readily than do simple alkyl halides.

3. When a mixture of two different vinyl compounds is polymerized, the resulting 'copolymer' molecules may contain a mixture of monomer units. The intermediate radicals may combine with either monomer. There will be four different propagation reactions, corresponding to reaction of the two different types of radical (with either kind of monomer at the radical end of the chain) with two different monomers. On the relative rates of these reactions depends the extent to which intermingling of monomers occurs in the resulting polymer, and by measuring the degree of intermingling it is possible to find the relative rates of the various propagation reactions.

Obviously the rate of a given propagation will depend on the reactivities of the corresponding radical and monomer, and so much useful information should be obtainable in this way. For example, polymerization of a mixture of butadiene and vinyl acetate gives almost pure polybutadiene. Therefore butadiene must react much more readily with radicals than does vinyl acetate. This we should expect to be the case; the reactivity of a given monomer varies with the resonance energy of the resulting radical, and the allyl radical resulting from addition to butadiene has a much larger resonance energy than the α-acetoxyl radical from vinyl acetate.

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† Lewis has obtained constants for vinyl acetate which agree with those of Swain and Bartlett but not with those of Burnett and Melville. This work was reported briefly at a recent Faraday Society Discussion.

Recently Mayo, Lewis, and Walling[†] have reported very extensive data on copolymerizations. Their investigation gives the ratio of the rates at which a given radical adds the two monomers. Now the rate at which the radical adds a monomer similar to that present in the radical end of the chain should be equal to the rate of propagation in the simple polymerization of that monomer. Thus in a copolymerization of vinyl acetate with vinyl chloride, the rate of addition of vinyl acetate to a radical ending in the group $\sim\!\sim\!\sim\mathrm{CH_2}\text{—}\dot{\mathrm{C}}\mathrm{HOAc}$ should be the same as the rate of propagation in the polymerization of pure vinyl acetate. Hence, using the data of Mayo, Lewis, and Walling together with the absolute values of propagation for vinyl acetate, styrene, and methyl methacrylate, it is possible to calculate the absolute rates of addition of radicals of the type

$$\sim\!\sim\!\sim\mathrm{CH_2}\cdot\dot{\mathrm{C}}\mathrm{HOAc}$$

$$\sim\!\sim\!\sim\mathrm{CH_2}\cdot\dot{\mathrm{C}}\mathrm{HPh}$$

$$\sim\!\sim\!\sim\mathrm{CH_2}\cdot\dot{\mathrm{C}}\mathrm{Me}\cdot\mathrm{COOMe}$$

to various ethylene derivatives. Values so calculated by Bamford are given in Table 30.

The rate of addition of a radical to a vinyl compound will be determined mainly by the resonance energy of the reactant and product radicals. Therefore the relative rates of reaction of a given radical to a variety of monomers provides a measure of the stability of the product radicals. Thus the reaction of each radical in Table 30 with styrene is much faster than the corresponding reaction with vinyl acetate; this must mean that phenyl is a more efficient radical-stabilizer than acetoxyl, the radical

$$\sim\!\sim\!\sim\mathrm{CH_2}\cdot\dot{\mathrm{C}}\mathrm{HPh}$$

having a larger resonance energy than $\sim\!\sim\!\sim\mathrm{CH_2}\cdot\dot{\mathrm{C}}\mathrm{HOAc}$.

Evidently a great deal of valuable information will be available when the data are more complete; but we may already deduce that +E substituents are the most effective radical-stabilizers, in agreement with the general theory. A more qualitative survey[‡] suggests that the order of activity is

$$\mathrm{CH{=}CH_2} > \mathrm{Ph} > \mathrm{CN} \sim \mathrm{COOMe} > \mathrm{Cl} > \mathrm{CH_2R} > \mathrm{AcO} > \mathrm{H}.$$

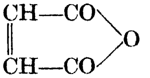
Other conclusions from this work are that compounds with a free methylene, $\mathrm{R_2C{=}CH_2}$. react more rapidly than analogous compounds in which substituents are attached to both ends of the double bond; that the different monomer units tend to alternate in a copolymer; and that *trans* isomers react more rapidly than *cis*. The theoretical interpretation of these facts is still not quite certain.

[†] *J.A.C.S.* 1948, **70**, 1529.

[‡] Nozaki, *J. Polymer Science*, 1946, **1**, 455.

TABLE 30

Velocity constants for reactions at 60°, *in litre mole*$^{-1}$ *sec.*$^{-1}$

Monomer	*Radical type*		
	—$\dot{C}$HPh	—$\dot{C}$HOAc	—$\dot{C}$Me·COOMe
$Ph\cdot CH{=}CH_2$	59	$2{\cdot}6\times 10^5$	386
$CH_2{=}CH\cdot CH{=}CH_2$	75	..	710
$MeOOC\cdot CMe{=}CH_2$	114	$1{\cdot}8\times 10^5$	177
$Me\cdot CO\cdot CH{=}CH_2$	203	..	..
$NC\cdot CMe{=}CH_2$	197	..	265
$NC\cdot CH{=}CH_2$	147	$4{\cdot}3\times 10^4$	131
$ClCH_2\cdot CH_2\cdot OOC\cdot CH{=}CH_2$	109	..	..
$MeOOC\cdot CH{=}CH_2$	79	$2{\cdot}6\times 10^4$	..
$Cl_2C{=}CH_2$	29·5	$2{\cdot}6\times 10^5$	70
$ClCH_2\cdot CMe{=}CH_2$	2·7	$2{\cdot}0\times 10^4$	24
$AcO\cdot CH_2.CMe{=}CH_2$	0·83	..	18
$ClCH{=}CH_2$	3·5	$1{\cdot}1\times 10^4$	14
$AcO\cdot CH{=}CH_2$	1·1	$2{\cdot}63\times 10^3$	8·9
$EtO\cdot CH{=}CH_2$	0·66	$8{\cdot}8\times 10^2$	..
$ClCH_2\cdot CH{=}CH_2$	1·9	..	4·3
$AcO\cdot CH_2\cdot CH{=}CH_2$	0·66	$4{\cdot}4\times 10^3$	7·7
	5,900	..	..
Ethyl fumarate	197	$2{\cdot}4\times 10^5$	..
Ethyl maleate	9·1	$1{\cdot}5\times 10^4$	8·9
$Cl_2C{=}CHCl$	4·5	$4{\cdot}0\times 10^3$	2·3
trans-dichlorethylene	1·8	$2{\cdot}7\times 10^3$	..
cis-dichlorethylene	0·26	$4{\cdot}2\times 10^2$	..
$Cl_2C{=}CCl_2$	0·32	$3{\cdot}9\times 10^2$	..

The 'double-bond' mechanism

Melville† has observed that when methyl methacrylate vapour is photopolymerized, polymerization continues for a considerable period after the light is cut off, and Bolland and Melville‡ have observed a similar effect in the vapour-phase polymerization of chloroprene ($CH_2{=}CCl{-}CH{=}CH_2$). Melville attributes this effect to an alternative mode of polymerization in which the chain centres are not radicals or ions, but 'activated double bonds' whose nature is not further specified. He represents the polymerization as

$$R_2C\overset{*}{=}CH_2 + R_2C{=}CH_2 \rightarrow R_2CH{-}CH_2{-}CH\overset{*}{=}CR_2$$
$$\xrightarrow{+R_2C=CH_2} R_2CH{-}CH_2{-}CH_2{-}CR_2{-}CH\overset{*}{=}CR_2 \quad \text{etc.,}$$

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† *Proc. Roy. Soc.* 1937, A **163**, 511.

‡ *Proc. Rubber Tech. Conf.*, London, 1938, 239.

where the asterisk indicates the 'activated double bond', and addition takes place with migration of hydrogen.

Now if we examine this mechanism more closely its improbability is at once apparent. A double bond can be activated only by excitation to a high-energy state. If the transition were an allowed one, the lifetime of such an excited state would be of the order of 10^{-8} sec., while even a metastable excited molecule, e.g. a triplet excited state (cf. p. 318), could hardly persist for as much as a tenth of a second in a condensed system (the polymerizations studied by Melville take place in a film of polymer deposited on the walls of the reaction vessel). Yet Melville claims that his 'active centres' can survive for days or even weeks without serious loss of activity. Moreover, although molecules do show unusual reactivity when excited by light, the reactivity is generally due to the production of free radicals, and not to energy-chain mechanisms of the type postulated by Melville. Certainly much more convincing evidence would be necessary before such radical innovations could be accepted into the general theory.

Actually Bamford and Dewar† have found that methyl methacrylate forms a catalyst when irradiated with ultra-violet light; the long-lived polymerization is undoubtedly a normal radical-chain process initiated by this catalyst. A similar interpretation will probably be found to hold in the case of chloroprene.

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† Unpublished work. See *Faraday Society Discussion on the Labile Molecule*, 1947.

CHAPTER XV

LIGHT ABSORPTION AND COLOUR

THE general principles of molecular spectroscopy are now familiar. A molecule can exist in a number of discrete energy states, and can pass from one to another by emitting or absorbing light of the requisite energy. If the states differ by an amount of energy ΔE, the frequency (ν) of the light absorbed or emitted during the transition is given by $h\nu = \Delta E$, where h is Planck's constant.

The total energy of a molecule can be divided into electronic (binding) energy and kinetic energy. Both are quantized; that is to say, the amount of each form of energy in the molecule is limited to certain definite values. Absorption or emission of light may accompany transitions in which the molecule changes either its electronic energy or its kinetic energy or both.

The spacing of energy-levels differing only by one or more quanta of kinetic energy is generally much closer than the spacing between adjacent electronic levels. Therefore transitions in which the electronic energy remains constant require smaller changes in total energy, and the emission or absorption of light of correspondingly lower frequency, than do electronic transitions. Such *vibration-rotation spectra* lie in the infra-red region of the spectrum. By studying them it is possible to learn much about the modes of vibration and rotation of molecules and hence about their dimensions and the force constants of the bonds in them. This information is of great value, but it does not directly concern us here. The infra-red spectra of molecules depend, as do their entropies, on their modes of vibration and rotation as a whole, and are therefore not predictable in any simple way from their electronic structures. Similar remarks apply to Raman spectra which likewise involve only kinetic energy transitions.

The present treatment is therefore restricted to electronic spectra—and further to absorption spectra, since it is rarely possible to excite emission spectra of organic molecules. Electronic absorption spectra are due to transitions from the ground state to an excited state; since such transitions may be accompanied by changes in vibrational or rotational energy, an electronic transition generally gives rise to a complex series of bands rather than to a single line. The frequency of each series of bands then tells us directly the difference in energy between one excited state of the molecule and its ground state. In practice, the first absorption band of a molecule is the most important, i.e. the band which occurs at the lowest frequency, and which is due to a transition to the lowest excited level. The previous discussion has confined our attention to the effect of structure on the ground-state energy of molecules. To interpret light absorption it is necessary to know how structure affects the energies of excited states, and particularly of the excited state of lowest energy.

Excited states of molecules ; general principles

In an unconjugated molecule the electrons are more or less localized in definite bonds, i.e. in diatomic molecular orbitals. To each 'normal' bond orbital there will correspond a series of excited orbitals, and excitation of a bonding electron to any of these will be accompanied by absorption of light. Such a transition will involve one bond only to a first approximation; the excited states of a single unconjugated σ- or π-bond may therefore be considered first.

The atoms linked by such a bond each have a series of atomic orbitals of higher energy than those used in forming the bond orbital. From such high-energy atomic orbitals a series of high-energy molecular orbitals can be constructed, just as the normal bond orbital is derived from ground-state atomic orbitals. There is, however, another type of excited molecular orbital which generally has a lower energy than the orbitals constructed from excited atoms, and which is therefore of more interest in the present connexion.

The formation of a molecular orbital from two atomic orbitals is closely akin to the process of hybridization (p. 7). A set of atomic orbitals in an atom can be replaced by an infinite number of other equivalent sets built up from linear combinations of the first, the only requirements being that they should satisfy certain mathematical conditions and that the total number of orbitals should be the same as in the original set so that their 'volume' or the number of electrons they can hold shall be the same. Now a simple molecular orbital can be expressed approximately as a linear combination of two atomic orbitals; it therefore exactly parallels a hybrid orbital. The atomic orbitals in the latter case derive from one atom, in the former from two different atoms. Therefore it should be possible to construct *two* molecular orbitals from the same pair of atomic orbitals, just as two atomic orbitals of one atom give rise to pairs of hybrid orbitals. What have previously been described as molecular orbitals are therefore only the lower-energy members of pairs of molecular orbitals; and excitation of an electron from the normal bond orbital to its high-energy partner should take place with absorption of light.

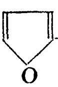
It might appear at first sight that this argument implies the possibility of combination between saturated molecules; thus two molecules of water might combine to form H_4O_2 by fusion of two atomic orbitals in the two oxygen atoms to give a pair of molecular orbitals capable of holding the four electrons originally present in the atomic orbitals. Since such compounds are not formed, it is evident that the energy liberated by forming the normal bond must be more than counterbalanced by the energy absorbed in forming the excited bond. The two molecular orbitals must therefore differ by at least the total binding energy (ΔE) of the normal bond, so that the energy liberated by placing two electrons in the normal bond orbital is less than the energy lost in forcing two electrons into the excited bond orbital. Actually the energy difference is considerably greater. Thus the C—C binding energy in ethane is about 81 Cals., but the first absorption band, corresponding to the transition of one electron from the bonding to the higher or *antibonding* orbital, lies in the vacuum ultra-violet at about 1,300 A and corresponds to an energy difference† of 220 Cals./Mol. There seems, however, to be a rough correlation between binding energy and energy of excitation to a corresponding antibonding orbital, weak bonds tending to absorb at lower frequencies (an effect seen very clearly in the halogens).

Excitation of σ-bond electrons generally requires very large energy changes in carbon compounds and the corresponding absorption bands lie in the vacuum ultra-violet, a part of the spectrum difficult to investigate. But similar excitation of π-electrons to antibonding π-orbitals takes place at much lower frequencies, the binding energy of π-electrons being less than that of σ-electrons. Thus ethylene has its first absorption maximum at 1,800 A and absorbs measurably up to 2,000 A.

Effects of conjugation

In the ground state of butadiene the four π-electrons occupy two extended orbitals covering all four nuclei. The same arguments lead us to suppose that two antibonding orbitals can also be constructed from the same four atomic orbitals and that excitation of bonding electrons to those should lead to light absorption. Similarly in a polyene with $2n$ conjugated atoms there will be n bonding orbitals, normally occupied by the $2n$ π-electrons, and also n antibonding orbitals which can take part in light absorption. The first absorption maximum will be due to a transition of one of the highest energy bond electrons to the lowest antibonding level. Both theoretical calculations and practical measurements show that in a series of analogous compounds differing only in the number of conjugated

TABLE 31

n	$CH_3\cdot(CH{=}CH)_nCOOH$	 $-(CH{=}CH)_n\cdot CHO$	$Ph-(CH{=}CH)_n-Ph$
0	..	2,730	2,520
1	2,010	3,150	3,180
2	2,510	3,510	3,520
3	2,910	3,740	3,770
4	3,240	..	4,040
5	..	..	4,340
6	..	..	4,580
7	..	..	4,740
11	..	..	5,300
15	..	..	5,700

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† Light of wavelength 3,000 A corresponds to an energy of 100 Cals./Mol. It is common practice nowadays to give the wave-number of light rather than its wavelength, the wave-number being the number of waves per cm., or ν/c. The energy of light of wave-number $\bar{\nu}$ is approximately $3\bar{\nu}$ cals./Mol. Visible light occupies the region $\bar{\nu} = 13000-28000$.

double bonds, the energy difference between the highest occupied and lowest unoccupied orbitals is less, the larger the conjugated system. Thus butadiene absorbs at lower frequencies than ethylene, hexatriene than butadiene, and so forth. The first absorption maxima for several series of 'vinylogues' are given (in A) in Table 31.

Aromatic compounds

In benzene, as in hexatriene, the six π-electrons occupy three bonding π-orbitals, and again there are three antibonding orbitals, excitation of electrons to which can lead to absorption of light. The situation is somewhat complicated by the fact that transition to the lowest excited state is 'forbidden' by symmetry considerations and leads only to very weak light absorption. The limit of absorption is at about 2,800 A compared with 2,000 A in ethylene, but the first intense band in benzene is at 2,000 A, only 200 A more than the first maximum in ethylene.

TABLE 32†

Compound	*First absorption maximum* (A)	
	Obs.	*Calc.*
Benzene	2,590	2,450
Diphenyl	2,515	..
p-Terphenyl	2,800	..
p-Quaterphenyl	3,000	..
p-Quinquiphenyl	3,100	..
p-Sexiphenyl	3,175	..
m-Terphenyl	2,515	..
m-Noviphenyl	2,530	..
m-Quindeciphenyl	2,540	..
Naphthalene	2,750	2,950
Anthracene	3,700	3,650
Naphthacene	4,600	4,500
Pentacene	5,800	5,450
Phenanthrene	2,950	3,000
Pyrene	3,300	3,450
Fulvene	3,650	3,645
Azulene	7,000	6,914
Butadiene	2,100	1,900

† Forster, *Z. phys. Chem.* 1938, B **41**, 304; *Z. Elektrochem.* 1939, **45**, 548; Gillam and Hey, *J.C.S.* 1939, 1170; Sklar, *J. Chem. Phys.* 1937, **5**, 669.

Following the general principle that increased conjugation in similar compounds leads to absorption at lower frequencies, it may be expected that polynuclear aromatic compounds on the one hand, and conjugated polyphenyls on the other, should absorb at lower frequencies than benzene. This is found to be the case (Table 32). It is particularly striking that the *m*-polyphenyls, where extended conjugation is not possible, do not absorb at lower frequencies than diphenyl. (The absorption bands of the polyphenyls are analogous to the strong benzene band at 2,000 A, not to the weak bands at 2,500–2,600 A.) Furthermore, sterically hindered diphenyls, where substituents prevent the coplanar configuration necessary for conjugation between the rings, have absorption spectra analogous to benzene rather than to diphenyl. In Table 32 wavelengths of the first absorption bands calculated by quantum mechanics are also given. The agreement between the calculated and observed values is extremely good. Indeed, the mathematical treatment has here far outstripped any qualitative theory, for it correctly predicts the remarkable differences between azulene (which absorbs strongly in the visible region and is intensely coloured) and naphthalene (which absorbs only in the ultra-violet), and between fulvene (which is again coloured) and hexatriene or benzene, differences for which no convincing qualitative explanation has been given.

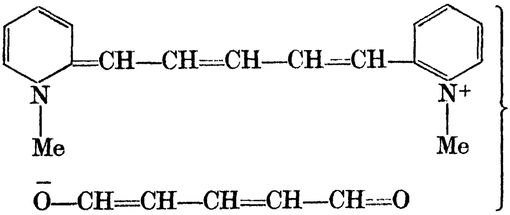
Cyanine dyes

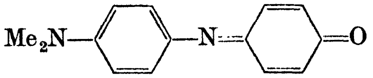
Cyanine dyes are a special class of polyenes where a cationoid group is attached to one end of the chain and an anionoid group to the other. The substituents conjugate with each other through the chain, forming an extended mesomeric system. A simple example is the dye-cation (I), formed by ring-fission from acylpyridinium salts and aniline, which we can picture as built up from an anionoid PhNH— group, a cationoid $\mathrm{Ph}\overset{+}{\mathrm{N}}\mathrm{H{=}CH}$— group, and a butadiene chain.

$$(\mathrm{PhNH}{\cdots}\mathrm{CH}{\cdots}\mathrm{CH}{\cdots}\mathrm{CH}{\cdots}\mathrm{CH}{\cdots}\mathrm{CH}{\cdots}\mathrm{NHPh})^{+}$$

(I)

The following are examples of cyanine dyes with various charge distributions; they have been written in their classical forms to emphasize the general make-up, but of course they are actually mesomeric.


true cyanines


Merocyanine

The true cyanine dyes are of especial interest because Brooker and his collaborators[†] have studied them in great detail and have clarified the relation between their colour and constitution.

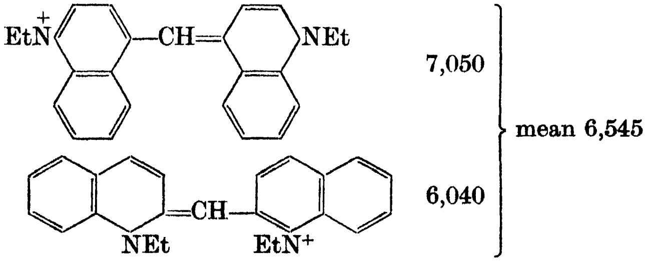
These compounds absorb at much lower frequencies than normal polyenes, and members of the series containing only two or three double bonds are already coloured. A quantum-mechanical explanation of this difference has been given;[‡] the qualitative interpretation of the quantitative treatment is roughly this. The sum of all the π-orbitals, bonding and antibonding, in a molecule must add up to the same total as the atomic orbitals from which they were formed. If, therefore, the bonding orbitals are not symmetrical, some atoms having more charge than others, some atomic orbitals will contribute more than others to the bonding π-orbitals. The antibonding orbitals must be unsymmetrical in the opposite sense, being formed from the residues of atomic orbitals left over from constructing the bonding orbitals. Therefore light absorption leads to a displacement of electric charge. Now quantum theory leads to the conclusion that the greater this charge displacement and the greater the distance in space over which the charge is displaced, the lower the frequency of light absorbed in the transition. This result is easily pictured in classical terms if we regard the light absorption as setting up a vibration of the charge between the two positions; the frequency of vibration would be less, the greater the charge or the greater the displacement in space. Now, cyanines consist of mesomeric ions where the charge will reside mainly on the terminal hetero atoms; these ions are therefore much less symmetrical than corresponding uncharged polyenes, the π-electrons being unevenly shared between the terminal hetero-atoms and the chain. Therefore light absorption produces a much greater charge displacement and the absorption occurs at lower frequencies.

[†] For a summary see Brooker, *Rev. Mod. Phys.* 1942, **14**, 275, see also *J.A.C.S.* 1945, **67**, 1869 et seq.

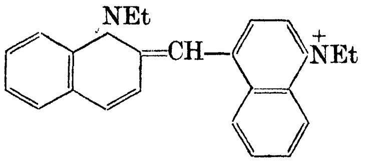
[‡] Herzfeld and Sklar, *Rev. Mod. Phys.* 1942, **14**, 294.

The effect will be greater, the more the charge is localized on the terminal atoms. Hence in a series of analogous symmetrical cyanines, the light absorption will be shifted to lower frequencies by an increase in anionoid activity, or 'basicity', of the terminal groups, or by an increase in cationoid activity of the chain. Moreover, lengthening the polyene chain will increase the distance over which charge is displaced, and so lead to a decrease in absorption frequency. The latter effect is of course very well known in the cyanine series; the former is less easy to establish because the terminal groups in ordinary cyanines form part of subsidiary mesomeric systems, and varying these will alter the absorption frequency, quite apart from any consequence of altered basicity.

So far it has been assumed that both terminal groups are the same, so that the dye-molecule is completely symmetrical. If the terminal groups differ, the absorption shifts to higher frequencies. Brooker demonstrated this effect in the following way. Fisher and Hamer[†] found that many unsymmetrical cyanines absorb at a wavelength which is the mean of the wavelengths for the corresponding symmetrical dyes, e.g.



[†] *Proc. Roy. Soc.* 1936, A **154**, 703.



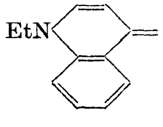
6,550

Fisher and Hamer used strongly basic terminal groups; Brooker found that if the terminal groups differed much in basicity the unsymmetrical dye absorbed at smaller wavelengths than the calculated mean of the symmetrical dyes. The difference between the observed and calculated wavelengths is a measure of the asymmetry effect mentioned above; Brooker calls it the *deviation*. In Table 33 a number of deviations for various unsymmetrical dyes are given.

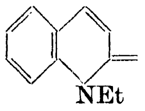
TABLE 33

Deviations of simple cyanines (one methine bridge)

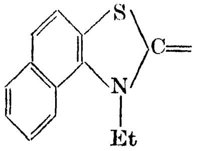
	A	B	C	D	E	F	G	H	I
A	(0)	(−5)	(−20)	15	0	220	380	615	730
B		(0)	20	30	15	145	255	410	525
C			(0)	(−5)	30	110	180	405	540
D				(0)	0	100	145	290	375
E					(0)	65	110	235	345
F						(0)	30	115	260
G							(0)	55	140
H								(0)	15
I									(0)



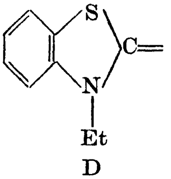
A



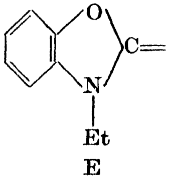
B



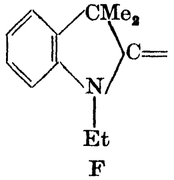
C



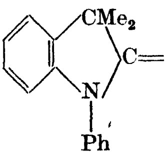
D



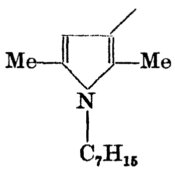
E



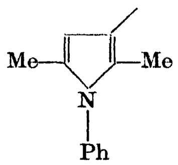
F



G



H



I

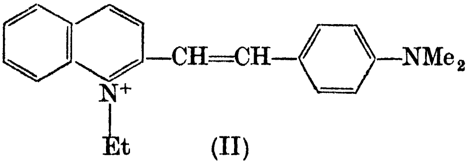
Order of basicity: A > B > C > D > E > F > G > H > I (it will be seen that the deviation is greater the farther the dye lies off the diagonal in the diagram, i.e. the greater the difference in basicity between its terminal groups).

Data from Brooker, Sprague, et al., *J.A.C.S.* 1945, 67, 1869, 1875, 1889.

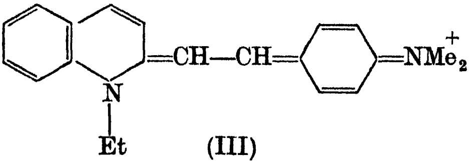
The theoretical interpretation seems to be this. If the dye is unsymmetrical, one terminal atom carries a lion's share of the ionic charge, and will then be held to the rest of the system by a bond of relatively low order. The whole conjugated system thus becomes unsymmetrical, alternate bonds having alternating orders. Light absorption is thus made difficult since the charge displacement accompanying it would alter the orders, and so the equilibrium lengths, of all the bonds in the chain, and hence the excited molecule would be formed in a strained configuration of high energy.† But if the molecule is initially symmetrical, the changes in bond-length due to a change in basicity of one terminal group are easily shown to be much smaller than if the molecule is initially unsymmetrical. Therefore small changes in basicity of one terminal group in a cyanine have little effect if the cyanine is initially symmetrical, but a large effect if it is highly unsymmetrical. This is seen to be the case from the data in Table 33; thus replacement of α-quinolyl (B) by the almost equally basic α-benzthiazolyl nucleus (D) has little effect in the symmetrical dyes, but a large effect when the other terminal group is very weakly basic (e.g. phenyldimethylpyrryl).

For efficient light absorption the dye should be sterically as symmetrical, and electronically as unsymmetrical, as possible.

Asymmetry will have the same effect however it is produced. Thus in the styrylquinoline derivative (II), mesomerism is made possible only by destroying the symmetry of both aromatic rings. The actual molecule therefore approaches the single form (II) closely and absorbs at high frequencies.‡ The stability of the other resonance form (III) could be increased by greatly altering the basicities of the terminal groups. Thus (IV) absorbs at much lower frequencies since the great basicity of NMe_2, relative to indole, counterbalances the resistance of the rings to becoming asymmetric. Likewise in (III) the deviation is large, in (IV) negligible.



(II)



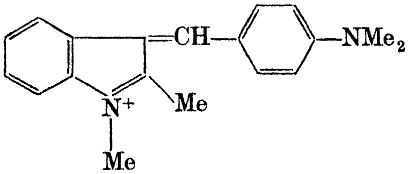
(III)

(5,270) (deviation, 820)

---

† Because absorption of light is a very rapid process compared with the periods of atomic vibrations in a molecule, so that absorption of light takes place without appreciable change in the positions of the nuclei (Franck–Condon principle).

‡ In the rest of this chapter the first absorption maximum (in A) is given under each formula. Wavelengths are given, rather than frequencies, since the former notation is more familiar to most chemists.



(IV)

(5,530) (deviation, —30)

Colour in organic chemistry

For a compound to be coloured, it must absorb visible light. The lowest excited level to which an electronic transition is allowed must be of relatively low energy. In organic chemistry coloured compounds are of three main types.

1. Compounds containing extensive polynuclear aromatic systems may absorb at sufficiently low frequencies to be coloured. Porphyrins, phthalocyanines, and polynuclear hydrocarbons like pentacene are good examples. These compounds have already been discussed.

2. Compounds containing the N=N bond are coloured, e.g. azomethane. Apparently a special type of excitation is involved. The antibonding N—N π-orbital differs relatively little in energy from an N atomic orbital, and light absorption takes place by excitation of an electron from an N atomic orbital to an N—N antibonding π-orbital. The energy of the latter can be lowered further by conjugation; hence azobenzene absorbs at lower frequencies than azomethane. The absorption of other double bonds at relatively low frequencies, e.g. N=O, can be explained likewise.

It is difficult to give any simple qualitative account of the detailed relationship between structure and colour in dyes of these two types; but in coloured hydrocarbons, at least, the absorption frequencies can be quantitatively calculated (cf. p. 298).

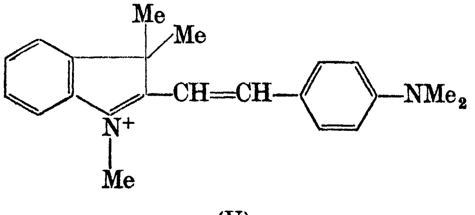
3. The third group of compounds are of the cyanine type, the two activating groups being attached to a complex mesomeric system in such a way that conjugation of the two groups with each other through the system is possible. The possibility of conjugation can be checked by the 'starring' method (p. 59). These compounds include all the remaining types of dyes. The same principles apply that Brooker has shown to hold for simple cyanines. Thus the absorption is shifted to lower frequencies by an increase in basicity of the terminal groups, by an increase in symmetry and degeneracy, and by an increase in the size of the conjugated system. The general principles will be illustrated presently by a survey of dyes, but one or two general points may first be raised.

±E substituents increase the size of the conjugated system; therefore they generally shift the absorption to lower frequencies (i.e. they exert a 'hypsochromic' effect). A proviso should be added, that +E substituents may, if suitably oriented, have the opposite (bathochromic) effect since they can also reduce the basicity of a terminal group or introduce cross-conjugation. —I substituents will also be hypsochromic since they will increase the basicity of the terminal groups, while +I substituents are bathochromic. Thus the group CF_3, which is strongly +I and has no E-activity, has a most powerful bathochromic effect. Halogens are also bathochromic as a rule, being strongly +I and weakly −E, while most other substituents are hypsochromic.

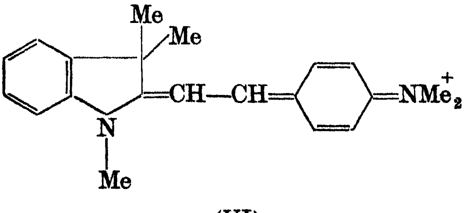
Secondly, a green dye is green because it absorbs red light. Since the energy of a quantum diminishes with wavelength, this must imply that green dyes have relatively low excitation energies. Now to each singlet excited state responsible for light absorption, there will correspond a triplet 'diradical' state of lower energy (cf. p. 318). Therefore in a green dye the triplet excited state may lie quite close to the ground state, and thermal excitation to it may take place with measurable speed at room temperature. Since the triplet state is a diradical, having two unpaired electrons, it should be more reactive than the normal state of the dye; therefore we might expect green dyes to be more fugitive than dyes of other colours, since excitation to the triplet state may lead to degradation. Green cyanine-type dyes are indeed notably fugitive.

1. Astraphloxin dyes

In dyes of the type (V), the difference in basicity of the terminal groups stabilizes the form (VI), while the tendency of the benzene ring to remain aromatic favours (V). The symmetry of the whole ion can be adjusted by varying the basicity of the terminal NR_2 group, and thus the position of light absorption can be varied. In such dyes, which are of considerable technical importance for dying acetate silk, the basicity is varied by using selections of the following groups, given in order of decreasing anionoid activity (and hence in order of increasing reduction of basicity of the amino group): Et > Me > $PhCH_2$ > $CH_2{\cdot}CH_2Cl{\cdot}$ > $CH_2{\cdot}COOH$.



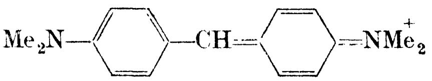
(V)



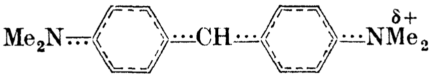
(VI)

2. Diphenylmethane and triphenylmethane dyes

Michler's Hydrol Blue (VII) is a normal cyanine dye where two double bonds in the polyene chain have been replaced by benzene rings. The rings are so placed that in the classical structure one is benzenoid, the other quinonoid; therefore cyanine mesomerism reduces the symmetry of the former but increases that of the latter, and since the two effects balance one another the dye is completely degenerate (VIII) and absorbs at low frequencies.†



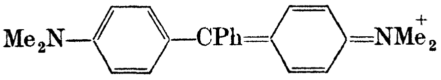
(VII)



(VIII)

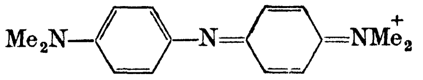
(6,035)

Any alteration in the structure of (VIII) which increases the tendency of the terminal nitrogen atoms to donate electrons to the central carbon chain will effectively increase the nitrogen basicity and so lower the absorption frequency. This may be brought about either by positive substitution of the central carbon (as in Malachite Green (IX) where the phenyl acts as a +E-substituent) or by replacing the central carbon by the more electronegative nitrogen as in Bindschedler's Green (X). Both these dyes absorb at lower frequencies than (VIII).†



(6,160)

(IX)



(6,400)

(X)

Moreover, substituents which increase the +E-activity of the central phenyl shift the absorption to still lower frequencies, while decrease in +E-activity has the opposite effect. This is illustrated by the first absorption bands of the substituted malachite greens quoted in Table 34.

It is interesting that *m*-OH behaves as a positive substituent (cf. p. 113).

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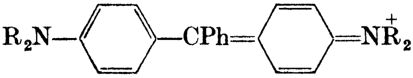
† In the rest of the chapter classical structures will generally be written for dyes, since the type of mesomerism in them is obvious.

TABLE 34

Malachite Greens with substituents in the central ring

Substituent	*First absorption band* (A)
o-NO_2	6,331
m-NO_2	6,357
p-NO_2	6,370
o-Cl	6,301
m-OH	6,174
(none)	6,160
p-OH	6,025
2:4-$(OH)_2$	6,010
p-Me	6,110
o-MeO	6,021
p-MeO	6,030
p-EtO	6,053

Altering the basicity of the terminal groups varies the light absorption in the same manner that it does in other cyanine-type dyes; increase in basicity leads to absorption at lower frequencies. Thus Dobner's Violet (XI) and its dimethyl (XII) and diethyl (XIII) derivatives absorb at higher frequencies than Malachite Green (IX), while the tetraethyl analogue, Brilliant Green (XIV), absorbs at lower frequencies.



(XI) $R_2N = NH_2$ (5,616)

(XII) $R_2N = NHMe$ (5,870)

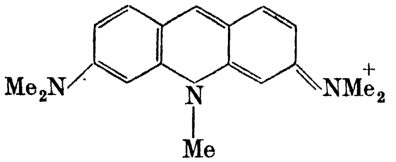
(XIII) $R_2N = NHEt$ (5,898)

(IX) $R_2N = NMe_2$ (6,160)

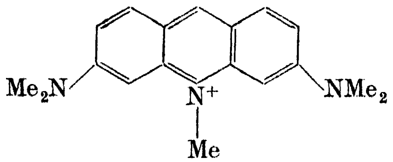
(XIV) $R_2N = NEt_2$ (6,230)

Introduction of a third basic group into Malachite Green gives Crystal Violet (XV), which absorbs at much higher frequencies. Crystal Violet has the completely degenerate structure (XVI) in which the charge on each nitrogen is roughly two-thirds that on the nitrogens in Malachite Green. Hence the charges migrating during light absorption are smaller and consequently absorption occurs at higher frequencies. In strong acid, one basic group of Malachite Green acquires a proton, and, since it no longer has a p-orbital available for conjugation, the resulting ion (XVII) resembles Malachite Green in structure and absorbs at correspondingly low frequencies. Actually it absorbs at lower frequencies than (IX) since the $\overset{+}{N}HMe_2$ group increases the +E-activity of the adjacent ring.

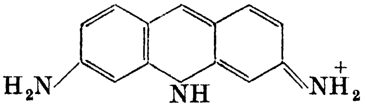
leads to an increase in resonance energy; the molecule therefore approximates to the structure (XXIII) which, unlike (XXII), contains an intact acridine ring-system.



(4,910)
(XXII)



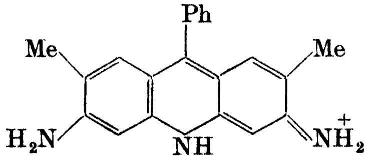
(XXIII)



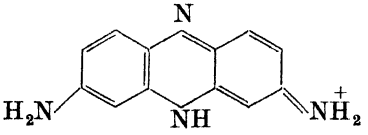
(4,270)
(XXIV)

Reducing the basicity of the terminal nitrogens shifts the absorption to still higher frequencies as in Proflavine (XXIV).

The light absorption of these dyes can be shifted to lower frequencies by any change in structure which increases the charges on the terminal amino groups. This can be done, firstly, by increasing the electron affinity of the central carbon by phenylating it (Benzoflavine, XXV) or replacing it by nitrogen (XXVI)

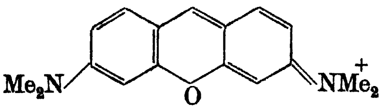


(4,580)
(XXV)

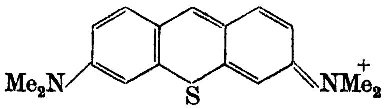


(5,130)
(XXVI)

Secondly, the basicity of the central nitrogen may be reduced by replacing it with the less basic atoms of oxygen (Pyronine G, XXVII) or sulphur (Thiopyronine, XXVIII). Both (XXVII) and (XXVIII) absorb at lower frequencies than (XXII).

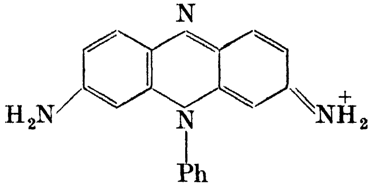


(5,475)
(XXVII)

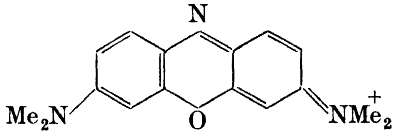


(5,645)
(XXVIII)

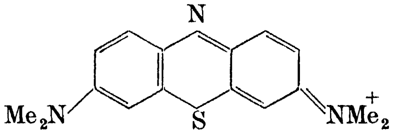
Thirdly, the absorption of the phenazine dyes (XXVI) can be shifted similarly to still lower wavelengths, either by phenylating the imino group or by replacing it with oxygen or sulphur. Phenosafranine (XXIX), Capri Blue (XXX), and Methylene Blue (XXXI) are examples.



(5,250)
(XXIX)

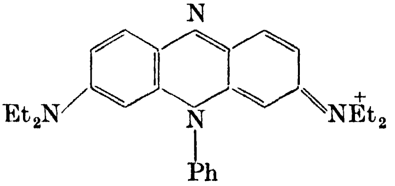


(6,489)
(XXX)

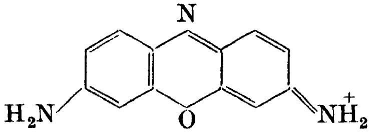


(6,084)
(XXXI)

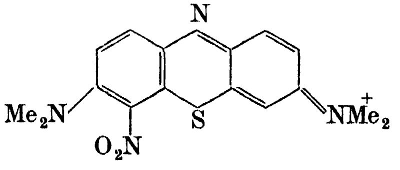
In all these dyes the absorption can be varied in the usual way by altering the basicity of the terminal nitrogens, as in Amethyst Violet (XXXII) or the dye (XXXIII).



(5,890)
(XXXII)



(5,868)
(XXXIII)

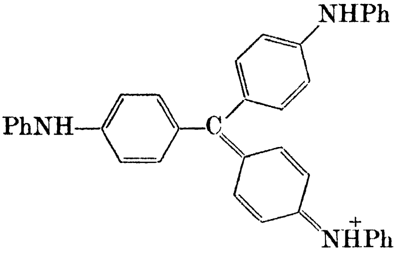


(6,580)
(XXXIV)

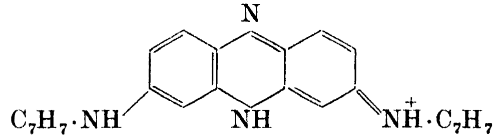
Yet another method of shifting the absorption to lower frequencies is to increase the cationoid activity of the central carbon chain by +E substitution, thus increasing the positive charges on the terminal nitrogen atoms. Methylene Green (XXXIV) is an example.

Effect of phenyl in the terminal amino groups

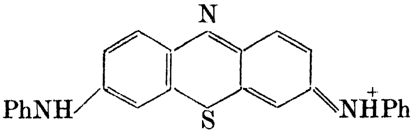
An exception to the usual rule, that lowering the basicity of the terminal amino groups shifts absorption to higher frequencies, is the deepening in colour brought about by terminal arylation; thus Diphenylamine Blue (XXXV) actually absorbs at lower frequencies than Crystal Violet (XVI), although the PhNH group is much less basic than Me_2N. Indazine M (XXXVI) and the dye (XXXVII) are good examples of the same effect.



(5,961)
(XXXV)

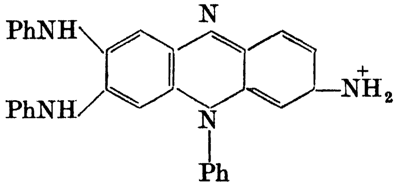


(5,720)
(XXXVI)

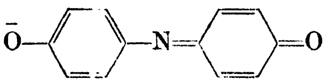


(7,000)
(XXXVII)

The extra aryl groups can of course conjugate with the terminal nitrogen atoms; the increase in conjugation shifts the absorption to lower frequencies and this effect outweighs that due to change in basicity. Even the unsymmetrical dye Indamine Blue (XXXVIII) evidently absorbs at remarkably low frequencies, judging by its blue colour.



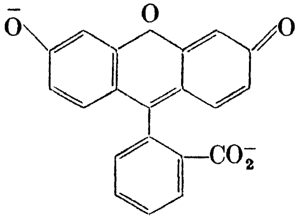
(XXXVIII)



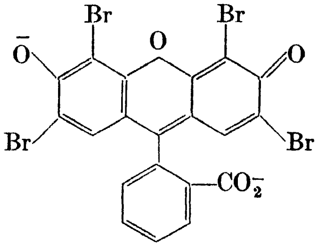
(6,300)
(XXXIX)

Acid dyes

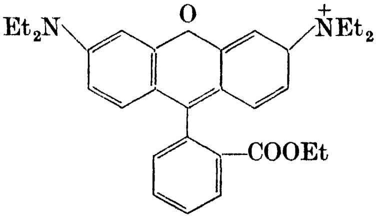
An exactly equivalent series of dyes are known containing mesomeric anions instead of cations. Here the anionoid terminal group is charged, the cationoid group uncharged. A simple example is the anion of phenolindophenol (XXXIX) which is an analogue of Bindschedler's Green (X). In these dyes the terminal groups carry a negative charge; therefore their absorption will be shifted to lower frequencies by any change in structure which increases the acidity (cationoid activity) of the terminal groups or reduces that of the intervening carbon chain. Thus Fluoresceine (XL) absorbs at higher frequencies than Eosine (XLI), since in the latter the acidity of the terminal oxygens is increased by the bromine substituents. It is interesting that in the analogous basic dyes a decrease in basicity of the terminal groups has its normal effect of shifting absorption to higher frequencies; as in Rhodamine 6G (XLII) and Rhodamine 3B (XLIII).



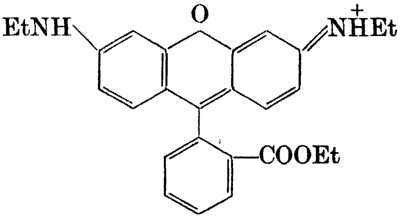
(4,890)
(XL)



(5,160)
(XLI)



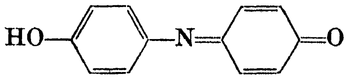
(5,526)
(XLII)



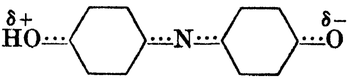
(5,193)
(XLIII)

Merocyanine dyes

A third class of cyanine-type dye is known, in whose classical structure neither terminal group is charged. Mesomerism then involves a separation of charges. The neutral form of phenolindophenol (XLIV) is a good example, the actual mesomeric structure being represented in (XLV).

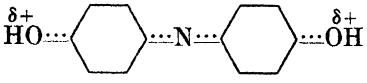


(4,950 in EtOH)
(XLIV)

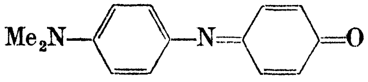


(XLV)

Here mesomerism is opposed by the separation of charges it requires (cf. p. 96). Hence the dye approximates to the classical structure (XLIV), and absorbs at much higher frequencies than the corresponding symmetrical anion (XXXIX) or the deep blue cation (XLVI) which is present in solutions of (XLV) in concentrated sulphuric acid (the Liebermann nitroso reaction depends on these colour relationships).



(XLVI)



(XLVII)

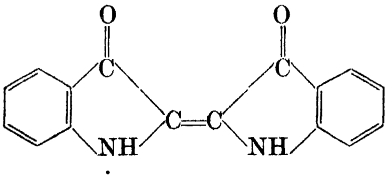
The absorption of merocyanine dyes should therefore be shifted to lower frequencies by any factor which favours the zwitterionic mesomer; by an increase in basicity of the anionoid terminal group, an increase in acidity of the cationoid terminal group, or an increase in dielectric constant of the surrounding medium. The latter effect is particularly striking since normal cyanines show much the same absorption in different solvents. The merocyanine Phenol Blue (XLVII), however, absorbs at much lower frequencies in solvents of high dielectric constant, as the following table† shows.

TABLE 35

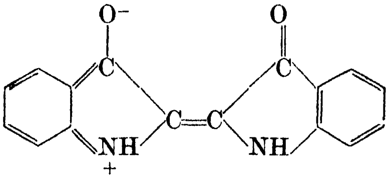
Absorption of Phenol Blue in solvents

Solvent	*Dielectric constant at 20°*	*First absorption band*
Cyclohexane . .	2	5,520 A
Acetone . . .	21	5,820 A
Methanol . .	34	6,120 A
Water . . .	80	6,680 A

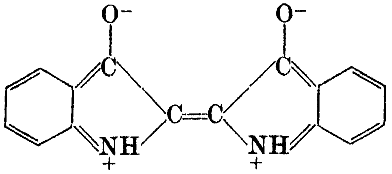
The most important merocyanine dyes are Indigo and the vat-dyes related to it. In Indigo mesomerism is possible between forms such as



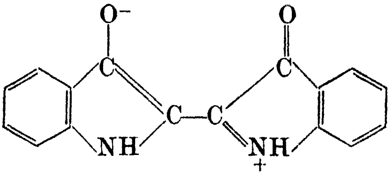
(*a*)



(*b*)



(*c*)



(*d*)

of which the forms of type (*d*) are probably the most important ionic ones since the central bond in indigo is exceptionally weak, *cis*- and *trans*-indigo isomerizing with unusual ease† (the central bond must therefore have a low order, and (*d*) is the only resonance form in which the central bond is single).

---

† Brooker and Sprague, *J.A.C.S.* 1941, **63**, 3214.

Indigo shows the normal merocyanine solvent effect (Table 36). The solid absorbs at very low frequencies since in it each indigo molecule is surrounded by highly polar dye molecules, and is therefore effectively embedded in a medium of high dielectric constant. Moreover, increase in basicity of the nitrogen atoms by methylation or nuclear substitution shifts the absorption to lower frequencies, substituents which lower its basicity having the converse effect; while substituents which increase the acidity of the CO groups likewise shift absorption to lower frequencies. Examples are given in Table 37. The nitroindigos are interesting; the positive effect of NO_2 is greatest in the *para* position, so a 5-NO_2 affects the nitrogen basicity more than the carbonyl acidity and therefore shifts absorption to higher frequencies, while a 6-NO_2 has the opposite effect.

TABLE 36

Absorption of Indigo in solvents

Solvent	*Dielectric constant at 20°*	*First absorption maximum* (A)
(Solid) . . .	. .	6,780
Aniline . . .	7·3	6,300
Acetic acid . .	6·4	6,159
Chloroform . .	5·0	6,048
Tetralin . . .	2·8	6,015
Xylene . . .	2·4	5,909
Vapour at 320° .	(1)	5,460

TABLE 37

Absorption of substituted Indigos

Substituents	*Solvent*	*First absorption maximum* (A)
(H). . . .	$CHCl_3$	6,048
(H). . . .	Xylene	5,909
N:N-dimethyl .	Xylene	6,445
5:5′-dimethoxy .	$C_2H_2Cl_4$	6,440
6:6′-dimethoxy .	$C_2H_2Cl_4$	5,770
5:5′-dinitro . .	$CHCl_3$	5,855
6:6′-dinitro . .	Xylene	6,355
7:7′-dimethyl . .	Xylene	6,038
6:6′-diethoxy . .	Xylene	5,185
N:N-dibenzoyl .	Xylene	5,780

Thioindigo (XLVIII) absorbs at higher frequencies than indigo since sulphur is less basic than nitrogen.

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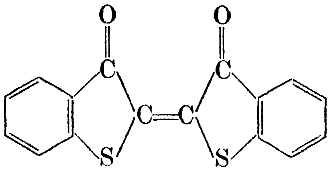
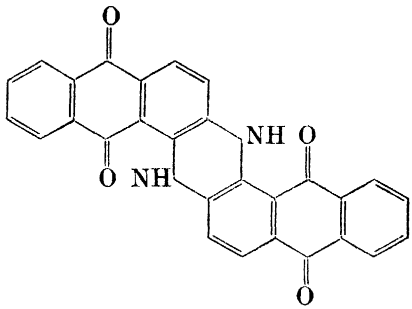
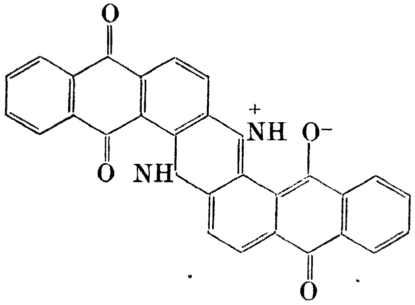
† Heller, *Ber.* **1939**, **72**, 1858.



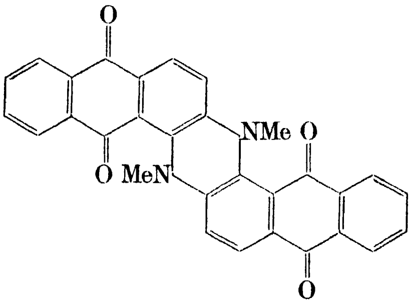
(5,435 in xylene)
(XLVIII)



(XLIX)

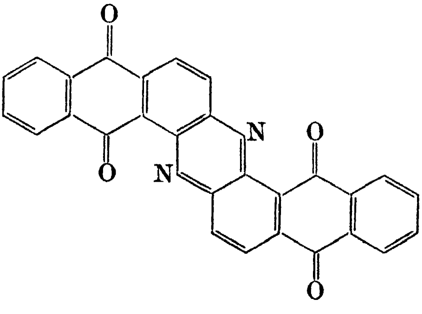


(L)



(7,000 in xylene)
(LI)

Indanthrene (XLIX) also absorbs at low frequencies, being deep blue in colour; mesomerism with forms such as (L) is possible and hence (XLIX) is a merocyanine like indigo. The N:N-dimethyl derivative (LI) absorbs, if anything, at lower frequencies than (L). Incidentally since the dimethyl derivatives have absorptions similar to those of the parent indigo and indanthrene, it is evident that hydrogen bonding plays no part in the colour of the latter. Probably the colour of other anthraquinone vat-dyes is due to similar merocyanine mesomerism. The colour is certainly not due merely to the presence of an extended aromatic structure, since the azine (LII) derived from (XLIX) by oxidation is weakly coloured (yellowish-green) although it contains an extra aromatic ring.



(LII)

Orientation and light-absorption

The majority of dyes of the cyanine type have flat elongated molecules with the charged groups at the ends of the long axis. Quantum-mechanical calculation shows that such a molecule should exhibit its low-frequency absorption only when the electric vector of the light lies along this axis. Since in many of these dyes the molecules in the crystal are oriented parallel to one another, a crystal of such a dye will absorb polarized light only when the electric vector of the light lies along a certain axis of the crystal. Such dye crystals are therefore strongly dichroic.

Since the molecule of the dye is planar and not linear, the π-orbitals in it have appreciable extension along the shorter axis as well as along the main cyanine axis. It can be shown that in such a system a second excited state is possible, excitation to which requires that the incident light be polarized with its vector along the shorter axis. Such a dye will then show a second absorption band (x-band) in addition to the normal long-wave absorption (y-band). The second excited state has a higher energy than the first and so the x-band occurs at higher frequencies than the y-band.

In oriented crystals polarized light of x-band frequency will be absorbed only if its vector lies along the shorter axes of the molecules. Hence when such a crystal is examined with suitably oriented polarized white light, it may show an absorption spectrum containing either the x-band alone or the y-band alone. All these phenomena have been observed and in certain cyanine dyes have been related to the orientation of the molecules in the crystal, determined by X-ray crystallography.

Many cyanine-type dyes show a third absorption band (z-band) in strong aqueous solution, generally at lower frequencies than the x- or y-bands. The z-band fades with dilution and is not usually observed at all in organic solvents. It has been shown that in the abnormal solutions the cyanine is highly polymerized, its flat molecules being stacked together into aggregates like packs of cards; and orientation experiments have shown that z-band absorption is exhibited only when the electric vector of the light lies along the pack, perpendicular to the x- and y-band axes. This must mean that some kind of chemical bond links the molecules together in the polymer, such that the π-orbitals in adjacent molecules overlap and fuse into an extended electronic system. The z-absorption is then due to excitation of one π-electron in this system, derived from the π-orbitals of all the component molecules, to a higher orbital. The mode of linkage is not known; but the heat of formation of the polymers is small ($<$ 10 Cals.) and is greater in water than in alcohol;† this suggests strongly that the polymers are really molecular complexes held together by dispersion forces (p. 184). (Dispersion forces between ions should be more effective in a polar solvent.) If so, considerable support is given to the idea that all forms of intermolecular attraction are qualitatively similar, the most general definition of a chemical bond being that it represents attractive interatomic forces. The apparent difference between covalent and electrovalent links on the one hand, and van der Waals' forces on the other, seems to be quantitative rather than qualitative, the latter being usually very much the smaller. When van der Waals' forces are abnormally large, as in molecular complexes or 'hydrogen bonds', they simulate all the properties of normal bonds. An accurate quantitative treatment would probably show that a continuous transition between the two types of bond is possible, just as present theory suggests a continuous transition between pure covalent and pure electrovalent links.

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† Rabinowitch and Epstein, *J.A.C.S.* 1941, **63**, 69.

Cis-trans isomerization†

The majority of organic reactions, apart from photochemical reactions, seem to be adiabatic; they involve no discontinuous electronic transitions. The interconversion of *cis-* and *trans-*isomers of certain olefines seems to be an exception.

In forming the π-bond in ethylene, two carbon p-orbitals overlap to form a π-orbital. Now the normal orbital is only the lower-energy member of a pair of π-orbitals that can be so constructed. If the molecule is not planar, the atomic orbitals will still give rise to a pair of π-orbitals, but their energies will differ from those of the orbitals in planar ethylene. The energy of the 'normal' orbital is least when the molecule is planar, greatest when the methylenes are at right angles (perpendicular ethylene), while the 'excited' orbital is most stable in the perpendicular form. The two molecular orbitals can be expressed in an infinite number of ways as (hybrid) linear combinations of the two simple π-orbitals. The actual ground state of the molecule will always be such that the π-electrons occupy the orbital of lowest energy available to them; and in a non-planar configuration one of the alternative hybrid orbitals will have a lower energy than either of the two simple π-orbitals. The energy required to twist one methylene group out of the plane of the original ethylene molecule will therefore be less than the energy that would be required if no hybridization occurred. If the methylene is slowly twisted through 90°, the π-electrons pass through a succession of such hybrid states into the original excited orbital which in perpendicular ethylene is more stable than the 'normal' orbital. Now such a twisting is the rate-determining step in the thermal *cis-trans* isomerization of an olefine; the perpendicular form may revert to the original structure or its isomer. This reaction can therefore take place by a continuous series of electronic transitions through an intermediate transition state of much lower energy than that required by a reaction where the π-bond was broken in the intermediate (corresponding to the π-electrons remaining throughout in the original 'normal' orbital, which in the perpendicular form has virtually no strength). A number of such isomerization reactions are indeed known which have normal frequency factors ($\sim 10^{12}$) and activation energies of about 45 Cals.—much less than the bond-energy of a C—C π-bond.

---

† See Magee, Shand, and Eyring, ibid. p. 677.

A second type of isomerization is possible, however. It has so far been assumed that excitation of one electron in ethylene to the antibonding orbital gives rise to only one excited state. But in the excited ethylene molecule the two π-electrons occupy separate orbitals. There is therefore no longer any necessity for their spins to be antiparallel. Accordingly there are two excited states of ethylene, one a singlet state in which the π-electron spins are antiparallel, the other a triplet where the spins are parallel. The latter has much the lower energy, but it does not contribute to light-absorption. To form it from normal ethylene, the spin of one π-electron would have to be reversed, and this is an improbable event. Therefore very few molecules which could otherwise absorb light of frequency suitable for the transition do in fact do so, and hence the absorption is too weak to measure; i.e. the transition is 'forbidden'. However, the most stable form of triplet ethylene is the perpendicular one, and so thermal excitation of ethylene to it can lead to *cis-trans* isomerization. Such a reaction should have an unusually small frequency factor, since the probability of the necessary spin-reversal is small and so only a small fraction of molecules satisfying the other conditions for inversion will actually react. It is, indeed, found that a second group of olefines invert by a reaction of abnormally small frequency factor ($\sim 10^5$) and with activation energies *c.* 25 Cals., much less than that required for the adiabatic reaction.

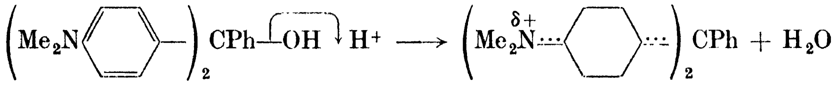
In both processes the activation energy will depend on the energy difference between the bonding and antibonding π-orbitals. The adiabatic reaction will be the more sensitive, since its absolute activation energy is greater and a change in the energy difference between the orbitals will affect it proportionately more. Since the energy difference is proportional to the excitation energy of the olefine, we should expect a parallel between the light-absorption of olefines and the mechanism by which they isomerize. The more conjugated an olefine, the more readily it will isomerize by the adiabatic mechanism, and the lower the frequency of its first absorption maximum. This is illustrated by the data in Table 38; the olefines which isomerize by the adiabatic process are the ones which absorb at the lower frequencies.

TABLE 38

Compound	*E for isomerization* (*Cals.*)	*First absorption max.* (A)
Maleic acid	15·8	2,100
Methyl maleate	26·5	2,100
Methyl citraconate	25·0	2,100
Butene-2	18·0	2,000
Methyl cinnamate	41·6	2,700
Stilbene	42·8	3,180
Monochlorstilbene	37·0	3,150

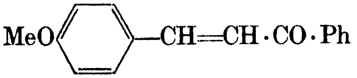
Halochromism

It has long been known† that certain colourless substances give coloured solutions with strong acids from which coloured salts of the parent compounds could often be isolated. The phenomenon, termed *halochromism*, attracted attention in the dye-era of organic chemistry and led to much speculation. The present interpretation is very simple. Halochromic compounds can be divided into two categories. In the first, acids bring about the dissociation of an alcohol by proton attack on the hydroxyl; the resulting carbonium ion is mesomeric and coloured, unlike the non-mesomeric alcohol. A simple example is the colourless 'leuco-base' (LIII) from Malachite Green (LIV), which gives salts of the latter with strong acid.



(LIII) (LIV)

Compounds of the second class are merocyanoid in structure; they contain an anionoid and a cationoid centre which are conjugated with each other through an intermediate unsaturated system. However, the activity of the centres is too low for the compounds to be appreciably degenerate and so they absorb at high frequencies, in the ultra-violet, and are colourless. When such a compound is treated with strong acids, it is the cationoid centre that combines with a proton since the merocyanoid mesomerism is sufficient to give it a partial negative charge. This salt-formation increases the cationoid activity of the centre so much that the resulting cation is far more degenerate than the parent base and hence it absorbs light of much lower frequency and is coloured. Anisalacetophenone (LV) is an example; its coloured solution in sulphuric acid presumably contains the more degenerate ion (LVI). It is interesting that compounds such as (LV) give coloured complexes with generalized acids such as $SnCl_4$; these presumably have structures like (LVII), the cationoid halide replacing the proton in (LVI).



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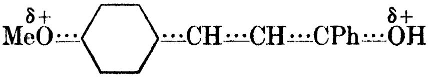
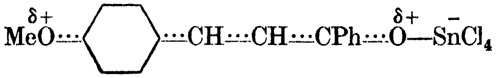


(LVI)



(LVII)

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† For numerous examples and references, see Pfeiffer, *Organische Molekülverbindungen*, Stuttgart, 1927.

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